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MULTIPLE GASTRIC POLYPOSIS

A Supplementary Report of 41 Cases, Including 3 New Personal Cases

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IN 1926, Brunn and Pearl (13), stimulated by the occurrence of successive cases, reviewed the subject of multiple polyps of the stomach, and collected from the available literature 78 cases having 3 or more polyps. To this they added 6 proved cases of their own and reported 7 probable cases, giving a statistical analysis from the more important viewpoints. In addition, they discussed at some length the incidence, diagnosis, symptoms, signs, pathology, and treatment of the disorder, which the reader may consult for details.

In that communication stress was laid on the elusiveness of gastric polyposis to the diagnostician, and a case was reported in which, despite their awareness resulting from intimate contact with literature and cases, the authors made an incorrect preoperative diagnosis. This case displayed a suggestive history, the usual laboratory findings of anacidity and bleeding, and the characteristic roentgenological picture (Fig. 1) of multiple gastric polyposis; but at operation was found a marked hypertrophic gastritis without polyps (Figs. 2, 3, 4). It is more probable that a correct diagnosis would have been made had gastroscopy been utilized in the investigation. In that article they also called particular attention to the difficulties in pathological diagnosis and classification of these growths, and to the incidence of malignant alteration of 12 per cent.

Notwithstanding our interest, 2 more cases of multiple gastric polyposis came to autopsy having eluded antemortem diagnosis, one of them (Case II)[1] even after a competent roentgenological examination. In addition, once again, as in our previous series, the diagnosis of multiple polypoid growths of the stomach was made in error on the basis of clinical, roentgenological, and laboratory evidence; but the stomach resected by one of us (H.B.) showed a marked hypertrophic gastritis (Case IV).

These misadventures aroused us to reconsider the entire subject of multiple gastric polyposis and induced one of us (F.L.P.) to collect from the literature all the additional cases of 3 or more gastric polyps reported since our previous compilation, appending the reports of our 3 recent cases (Table III). The data from these 41 cases will be presented as a separate series and the statistics compared, when indicated, with those of our previous inventory of 84 cases. Since the recent reports

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[1]Roman numerals refer to cases reported in text; Arabic to collected cases in Table III.

are much more complete than the early ones, their collected series will be far more trustworthy than the former group for statistical deduction.

INCIDENCE

Multiple gastric polyposis is not common. Previous data on incidence, however, are not reliable. Many cases are undoubtedly overlooked because of lack of symptoms. The authors were previously able to collect only 79 cases from 1820 to 1926, adding 5 of their own. From 1926 to 1941, however, they found 38 reported cases adding 3 of their own. This increase in incidence may be only apparent, reflecting a greater acumen in diagnosis and a willingness to report, rather than a true increase in frequency of the disease. Thirty of the 41 cases occurred in males. The youngest was 23, the oldest 80. Two-thirds of the cases were discovered in the 4th and 5th decades. This gives no information as to how long the condition was present, inasmuch as it may lie dormant for an indeterminate period.

ETIOLOGY

There are two recognized theories regarding the origin of multiple polyps of the stomach. One group, including Wechselmann and Rippert, is of the opinion that they are of congenital origin—true neoplastic growths. The occurrence of the disorder in twins, in 3, 4, and 6 siblings, in a mother and son, seems to support this contention. In our combined series of 125 cases, however, we have not found a single instance in which a familial predisposition was evident. It is otherwise with certain strains of mice. Stewart (105) reported the occurrence in the pyloric chamber of almost all his strain I mice of both sexes diffuse lesions characterized by adenomatous, hypertrophic, and hyperplastic overgrowth of glandular rugae. This is definitely inherited as a recessive character. The absence of well marked hereditary tendencies in our human cases and the almost universal appearance of hereditary adenomatous growths in these mice cannot now be correlated. Noteworthy is the difference between multiple gastric polyposis in which hereditary influence is questionable, and between colonic polyposis in which hereditary factors are strong.

A second group, among which are Cornil (23, 24), Menetrier (68, 69), and Verse, affirm that the growths are due to chronic inflammation. Konjetzny claims to have found all stages in the chain from hypertrophic gastritis to adenoma, and finally to carcinoma. Adenopapillomas have been produced by chronic irritation resulting from the use of nematodes and by other methods.

The relationship between gastritis, adenoma, and carcinoma, is now receiving considerable attention from the profession. The high incidence of achlorhydria in our series of cases of multiple polyposis indicated that the condition is associated with widespread changes in the function of the gastric epithelium; similar types of gastric secretion are found in over 60 per cent of cases of carcinoma. In 36 cases of multiple and single adenomas observed by Schindler through the gastroscope in 2,167 patients, 26 had a definite gastritis; of this number 20 were atrophic, 2 superficial, and 4 hypertrophic in type. Conversely, 0.83 per cent of 1,814 patients without atrophic gastritis had visible adenomas, whereas 6 per cent of 353 patients with atrophic gastritis had adenomas.

Inasmuch as patients with pernicious anemia regularly also have gastric achlorhydria, studies have been made to determine a possible relationship between pernicious anemia and multiple adenomas. Schindler found gastric adenomas in 6 of 43 patients suffering from pernicious anemia but did not mention whether they were single or multiple. This is a much greater incidence than that found in patients not having pernicious anemia. Rhoades notes that gastric polyposis is more common in cases dead of pernicious anemia than in those dead of other causes. Madelaine Brown (12) in a study of the stomachs at postmortem examination of patients dead of pernicious anemia found chronic gastritis regularly present. She also noted that the incidence of benign gastric tumors in 151 autopsies on patients dead of pernicious anemia was 8 per cent, whereas the incidence in 18,200 autopsies of patients without pernicious anemia was only 0.003 per cent.

It would be outside of the scope of this paper further to discuss the subject of gastritis as related to adenomas or carcinoma. The facts noted are only a small part of the evidence that a causal relationship may exist between gastritis, adenoma, and adenocarcinoma, and that atrophic gastritis may be the soil upon which neoplasm develops. Few believe, however, that all carcinomas are preceded by atrophic gastritis. In fact, of 47 cases examined both gastroscopically and microscopically by Schindler (99), a normal mucosa was found in 14 and chronic gastritis in 33. Research in this field is being hindered by the difficulty in producing adenomas experimentally. Most of the research in the experimental production of polypoid tumors by the use of irritants has been done in rats or mice and has resulted in the appearance of both benign and malignant polypoid tumors arising from the squamous epithelium of the forestomach. The adenoma and adenocarcinoma of the human stomach is analogous not to the tumors arising from the forestomach of mice, but from the pyloric canal which is lined by glandular epithelium. Rarely has adenoma been produced in this area by experimental means. Recently Klein and Palmer have set up minimum criteria which must be satisfied before any experimental tumor may be judged malignant. In a careful review of the literature they found no adenomatous lesion of the stomach which conforms to these criteria.

PATHOLOGY

According to Menetrier's classification of these growths (68, 69) there are two types—*polyadenome polypeaux* and the rarer *polyadenome en nappe*. In the former there are many discrete polyps scattered over the mucosa, usually pedunculated and bearing cysts. In the latter the hypertrophy forms a well demarcated plaque, not cystic or pedunculated, composed of closely placed folds of hypertrophic mucous membrane. Menetrier believes the *polypeaux* variety to be due to hypertrophic changes involving the ducts and necks of the glands, with the stalk and tumor pattern formed by connective tissue elements derived from the submucosa; the *en nappe* type is thought to be a more purely epithelial growth which involves the fundus of the glands. The *polyadenome polypeaux* conforms to the type which we consider as probably congenital, whereas the *polyadenome en nappe* fits the description of a localized hypertrophic gastritis. Menetrier, however, claims that both types are due to chronic inflammation.

The authors recognize two types of gastric polyps: (1) the congenital, neoplastic adenomas, and (2) the acquired hyperplasias due to chronic irritation. It is often possible to differentiate these two types of polyposis by the gross appearance. The adenomas are soft, dainty polyps, of various sizes, usually differentiated into head and stalk, of considerable height, and arising sharply from the mucosa. Some have thin stalks, others have broader based attachments. They are freely movable on the submucosa, and each tumor is isolated from the other by a strip of normal mucous membrane. The remainder of the gastric mucosa shows no signs of inflammation. On section the submucosa is seen to invaginate itself into the growth as a connective tissue core. The inflammatory hyperplasias have defective margins which merge into the normal mucosa. Their edges have a slow rise to a hilly slope, and they are flatter and more expansive on account of the inflammatory reaction. One does not receive the impression of an independent, suddenly arising, isolated tumor. They are firm and rest immovable on the submucosa. Inflammatory polyps are never differentiated into head and stalk, and on section the submucosa is found to take no part in the growth as a connective tissue core. The neighboring mucosa shows definite signs of chronic inflammation.

On microscopic examination the *neoplastic polyps* are seen to be composed of a glandular epithelium resting upon a central fibrous core. The core is composed of fibrous tissue which originates in the submucosa. The latter seems to invaginate itself into the center of the adenoma, pushing before it the muscularis mucosae which becomes split into strands and enters the stalk. The fibrous tissues may be edematous, containing thick or thin collagenous bundles. The epithelium is arranged in a disorderly fashion into glands which show

TABLE I.—SYMPTOMS AND PHYSICAL SIGNS—41 CASES

	No. cases present
Pain or distress	31
Anorexia	10
Nausea	8
Vomiting	14
Diarrhea	5
Hematemesis	7
Weakness	14
Constipation	6
Tumor	7
Tenderness	9
Rigidity	1*

*Perforated duodenal ulcer.

considerable variation from the normal. Many are elongated, tortuous, and dilated; some have been changed into small cysts containing old secretory material. At times the epithelial lining shows proliferation in the form of atypical papillae. Superficial ulceration and necrosis with inflammatory infiltration often occur. The epithelial cells may be of the undifferentiated, tall, hyperchromatic type; or of the type resembling the cells of the large intestine. There may be mixtures of goblet cells, Paneth cells, and the fuchsinophil cells of Lubarsch, with transitions from one to another, even in the same gland.

The *hyperplastic polyps* show a microscopic picture usually easily differentiated from the true fibroadenomas. The muscularis mucosae is always intact, and the submucosa makes no attempt to insinuate itself into the hyperplastic area to form a core. The enlargement which forms the "polyp" is composed of a purely mucosal proliferation in which the epithelial and fibrous components both play a part. The glands become hypertrophied, deeper, larger, and heavier, and the fibrous tissue becomes increased; but there is no irregularity in the fundamental character of the glandular and fibrous components or in their interrelationships. The undifferentiated, hyperchromatic cell is rarely seen. The epithelial cells may resemble those of the normal stomach for that area; or they may be replaced by the colonic type of cell. Cystic dilatation is less common. These hyperplastic areas are not sharply delineated, but merge imperceptibly into the adjacent mucosa. Inflammatory cells are generously disbursed throughout the hyperplastic area and the mucosa adjoining it.

In some cases both "neoplastic" and "hyperplastic" types may appear in the same specimen. At times the microscopic picture may not fit readily into the classification given, making it difficult, or even impossible, to place the abnormality in a clear-cut neoplastic or hyperplastic category.

Interesting is the fact that the condition of multiple gastric polyposis stops abruptly at the duodenum. In Case 32 duodenal involvement was diagnosed roentgenologically and at operation; but it is more probable that the surgeon felt gastric polyps prolapsed into the duodenum. Since no specimen was available, the proof of duodenal participation was lacking. We know of no case in which the condition was proved to include the duodenum.

SYMPTOMS AND SIGNS

There are no symptoms which are characteristic of this disorder. Epigastric pain or distress was the most frequent symptom, being present in 31 cases of this series. Hematemesis was present in 7. In 2 cases (Cases 1,7) it was the presenting symptom, in 1 (Case 1) it caused death. Evidence of bleeding, gross or occult, was found in the stools in 14 additional cases. In 5 cases gross bleeding was evident on examination of the stool. Thus bleeding was known to be present in 21 of the 40 cases. Diarrhea was noted in 5. It is probably the result of the achlorhydria which is such a common finding. In 2 cases it was the presenting symptom. For 25 years one patient (Case 2) suffered from diarrhea, which disappeared promptly following excision of the polyps. The frequent complaint of weakness (14 cases) is probably due to bleeding from ulcerated polyps. Fourteen complained of vomiting. The incidence of symptoms is indicated in Table I.

Pedunculated tumors are more apt to give symptoms than broad based ones. Tumors on a long, thin stalk may become detached, appearing in the vomitus (Case 31), in the gastric lavage water, or attached to a stomach tube used for diagnosis or treatment (13, 20, 47, 118); or they may be found in the stool (78). Indeed, the first antemortem diagnosis was made at operation in 1909 because of a piece of tumor tissue found attached to the stomach tube (118). The separation of polyps may

cause pain and bleeding. Tumors near the pylorus are more likely to cause spastic symptoms; one or a group of freely movable polyps may prolapse through the pylorus into the duodenum, thus producing partial or complete pyloric obstruction (13, 23, 25, 78) as in Cases 7, 16, 20, 33.

Some patients have had symptoms referable to the stomach for many years. Durations of 20 years or longer have been reported by Wegele—29 years; Menetrier (68)—25 years; Brunn and Pearl (13)—25 and 20 years; several others have had symptoms lasting over 10 years. Diarrhea was the only symptom in Case 2 for 25 years; it disappeared promptly after excision of the polyps. Sudden increases in severity of symptoms should warn one of the possible onset of malignant degeneration as in the case reported by Brunn and Pearl. Long remissions may occur.

In 7 cases a tumor mass was palpable. In our previous report, a palpable mass was noted in only 1 case. Tenderness was present in 9 cases. Rigidity was found in only 1 case, this being due to the associated perforation of a duodenal ulcer (Table I).

DIAGNOSIS

It is not surprising that a disease which may remain symptomless for so long should be so difficult to detect during life. At the time of our last report (13) we believed that the x-ray picture was so characteristic that the diagnosis could be made in the great majority of cases by roentgenography; it was then that we improperly diagnosed a case of hypertrophic gastritis as diffuse gastric polyposis (Figs. 1 to 4). It is clear from our experience that one cannot rely on the x-ray to make the differential diagnosis between multiple gastric polyps and hypertrophic gastritis. Food particles in the stomach, bezoars, and sarcoma may also be difficult to differentiate roentgenologically. In our recent series of 41 personal and collected cases, the correct diagnosis was made by x-ray in 17, by operation in 13, by examination of the excised surgical specimen in 5, and by autopsy in 6.

We have analyzed our series from the roentgenological standpoint, comparing the roentgenological diagnosis with the findings at operation or autopsy. It is somewhat difficult to evaluate the status of the x-ray in the diagnosis. Roentgenological reports are available in 36 cases. In 5 of these the main x-ray diagnosis was obviously incorrect. In the remaining 31 the main roentgenological diagnosis was correct as far as the essential lesion was concerned, but in 14 instances polyps were completely overlooked. For example in our Case II the roentgenologist diagnosed a diaphragmatic hernia, but overlooked typical filling defects of gastric polyps in the herniated cardia which were evident on retrospect examination of the films. In 11 instances the type of lesion was correctly diagnosed but the number of lesions reported by the roentgenologist was less than that found in the specimen. In 8 instances, the diagnosis was correct in type, but involved areas were missed. Lesions of the cardia more easily escape notice because pressure on the barium shadow is difficult. Occasionally the roentgenologist diagnoses polypoid tumors when only a marked hypertrophic gastritis exists. This occurred in a case report of Brunn and Pearl (13), and in Case IV. One must take into consideration that the cases in this series were collected from widely separated sources, and that the individual experience of reporting authors in this uncommon affection is not great.

Although the first case of gastric polyposis diagnosed by gastroscopy was reported in 1922 by Schindler (99), it is only recently that this method of diagnosis has come into more general use. The more frequent employment of gastroscopy in vague gastric disorders will undoubtedly increase the number of cases diagnosed during life. The gastroscope is particularly valuable in diagnosing mucosal lesions, and was responsible for the visualization by Dr. Allan Cohn of gastric polyps in our Case III, in which the roentgenologist interpreted the x-ray filling defects as due to retained food. There need be no rivalry between the 2 methods; each is complementary to the other, each has its limitations, and neither should be used to the exclusion of the other. The combined use of roentgenography and gastroscopy in the diagnosis of obscure gastric complaints will afford us more accurate diagnosis than we have ever known before.

TABLE II.—LABORATORY DATA

	Total cases examined	No. cases present
Gastric analysis		
No free hydrochloric acid	24	22
Blood	23	5
Tumor tissue	23	0
Myorrhea	23	4
Occult blood—stool	21	16
Anemia	21	15
Blood Wassermann—negative	10	10

The diagnosis of malignant degeneration of gastric polyps in the living subject is still an unsolved problem. The pathologist himself may be unable to settle this important question in the excised stomach, and in the microscopic preparations made therefrom. Unfortunately the stomach cells change very quickly after the blood supply has been arrested, thus confusing the microscopic picture. Too, pathologists often disagree as to the criteria of malignant alteration. Therefore, it is much to expect of the roentgenologist or the gastroscopist to diagnose malignant degeneration in borderline cases. Some gastroscopists claim their ability to make this differentiation by characteristics which are visible through the instrument but not apparent in the excised specimen or at autopsy. This will be a great step forward if their contention is upheld by further study. In certain cases, outspoken deep infiltration of the gastric wall is disclosed by the x-ray or the gastroscope. In our present series of 41 cases, only 27 gave satisfactory data on malignancy. Of these, the clinical diagnosis was correct as to malignancy or benignancy in 20 cases. Of the 7 cases in which the clinical diagnosis as to malignancy was incorrectly, 4 were erroneously diagnosed as benign, and 3 were erroneously diagnosed as malignant.

The examination of the gastric content is of great importance (Table II). Of 24 cases in which it was done, 22 had no free hydrochloric acid. The presence of anacidity in multiple polyposis is even more common than in carcinoma in which 60 per cent of patients had achlorhydria. In the examination of 70 specimens of gastric carcinoma from operation or autopsy, Brunschwig and associates found no correlation between the site, size, and histological type of the growth and the character of gastric secretion observed following the use of histamine. Blood was noted in our series in 5 cases. No tumor tissue was found in the gastric content, but this should not deter the examiner from making careful search for small tumor particles, especially in the specimens showing blood. The discovery of polypoid tumor tissue gives indisputable evidence of the presence of such tumors but not of their invasiveness. The latter condition can be judged only in specimens which contain the submucosa, in which alone malignant invasion can be demonstrated. In fact, Wegele made the first antemortem diagnosis at operation for a suspected carcinoma which he had erroneously diagnosed from a piece of tumor tissue expressed through the stomach tube. Thus in Case 14 malignancy could not be demonstrated in tumors removed for biopsy but was definite 4 weeks later at autopsy. The presence in the gastric content of fresh blood, associated with increased mucus is suspicious of the presence of gastric polyposis; if there is also an absence of free hydrochloric acid the diagnosis is much more probable. Conversely, one should hesitate to make this diagnosis in cases having considerable free hydrochloric acid in the fasting content. Brunn and Pearl (13) reported a case with known anacidity for 25 years. The cause and effects of this prolonged anacidity are poorly understood. Some claim that it is due to an initial atrophic gastritis and that hypertrophic gastritis, polyposis, and carcinoma are progressive stages in the development of the disease.

Even at operation the surgeon may have difficulty in diagnosing gastric polyposis in the unopened stomach. He may feel nothing abnormal (5, 31) or he may feel a thickened gastric wall, or the stomach may feel "like it contained worms." If the least doubt exists, the stomach should be opened and its mucosa directly inspected. If x-ray or gastroscopy has shown a defect, and nothing is found on palpation of the intact stomach, gastrotomy is mandatory. Too often instances are missed during life, to be found only in the postmortem room. One must not hesitate to advise a roentgenological and gastroscopic examination of the stomach in any case of gastric complaint which does not react promptly to the

usual measures. Severe gastric hemorrhage, the vomiting of increased quantities of mucus, or the persistence of occult bleeding in the stool without apparent cause are suggestive findings which demand a complete roentgenological and gastroscopic investigation by specially trained men.

TREATMENT

In the present series the surgical treatment consisted, for the most part, in (1) local excision of all polyps and (2) gastric resection. In a small number of cases resection was combined with excision of a few polyps remaining in the gastric stump. In one case (Case 38) polyps were removed by a diathermy snare through a gastrostomy (42). Medical treatment only was given in 3 cases, all of which terminated fatally, one from hematemesis (Case 1), one from alcoholism (Case 19), and 1 from streptococcus viridans septicemia (Case 22). A more detailed analysis from the standpoint of surgical treatment follows:

Local excision of all polyps. This procedure was carried out 8 times. Two patients died of the operation. Two were well up to 6 weeks after operation. Further details regarding the course of the individual cases are as follows:

Of the 4 benign cases, the results of local excision of the polyps were: Case 2, patient relieved (no dates); Case 10, patient died 2 days after operation from peritonitis; Case 17, patient well with a 16 pound weight increase 6 weeks after operation; Case 30, death after 1 year. Of the 4 malignant cases, the results of excision were: Case 13, patient died of pulmonary edema, 1 day after operation; Case 8, recurrence of pain, 3 months after operation; Case 21, patient was relieved for 5 years and then had an operation for recurrent polypoid tumors and died; Case 28, relief for 5 years, then recurrence of symptoms.

The short follow-up period in many of these cases makes any deductions unreliable. Of the 2 benign cases which survived the operation (Cases 2, 17) both were greatly improved, but whether malignancy supervened after the short observation period cannot be learned. The malignant cases made a poor showing. Not one had a satisfactory result. Two were relieved for 5 years (Cases 21, 28) before the return of symptoms and signs denoting recurrence of malignancy; in one of these, an extragastric gland showed no microscopic evidence of malignancy 7 years before. One is struck with the inadequacy of local excision in the treatment of multiple gastric polyposis and with the danger of making any prognostication even 5 years after operation.

Gastric resection was carried out 19 times. In Cases 23, 24, 36, one or more polyps were excised from the gastric stump. Four patients died of the operation, one in 3 days of severe anemia, one in 12 hours of pneumonia, 1 in 2 weeks of a complicating subphrenic abscess, and 1 in 5 days of peritonitis and jaundice. Five cases gave no follow-up data. Of the remaining 10 cases, 7 patients were alive and symptomless from 6 months to 4 years after operation. One other patient (Case 9) was alive 1 year after operation with probable liver metastasis, and one (Case 4) had a blood picture resembling pernicious anemia. Of the 19 patients treated by resection in 2 cases no malignancy data are given. Of the benign cases 2 (Cases 29, 34) died of the operation, one following a complete gastrectomy. The courses of the 9 benign cases are: Case 3, patient had uneventful convalescence (no dates); Case 4, patient's blood resembled that of pernicious anemia; Case 11, no data; Case 20, complete relief (no dates); Case 23, complete relief 7 months after operation; Case 25, no data; Cases 29 and 34, patients died of operation; Case 35, patient well 15 months after operation. Of the 8 malignant cases, 2 patients died of the operation (Cases 12, 41). The disposition of the 8 malignant cases is as follows: Case 7, patient well 1 year after operation; Case 9, liver metastases 1 year after operation; Case 12, patient died of operation; Case 24, patient had complete relief (no dates); Case 33, patient well 4 years after operation; Case 26, no data; Case 37, patient well 6 months after operation; gained 10 pounds; Case 40, patient died 5 days after operation of peritonitis and jaundice. Two cases gave no malignancy data.

Thus, of those which survived gastric resection, 4 of the 5 benign cases had a satisfactory result from 1 to 4 years after operation. In comparison, a satisfactory result was obtained

in 2 of the 3 benign cases (up to only 6 weeks) and in none of the 4 malignant cases which survived local excision. The authors emphasize the inadequacy in number and follow-up data of these cases, but the superiority of gastric resection as a routine method of treatment is strongly indicated. Most important is the fact that gastric resection eliminates the possibility of the onset of malignant degeneration such as occurs in the bases of excised polyps.

Biopsy. In 6 cases (Cases 5, 6, 14, 15, 16, 38) one or more polyps were removed through a gastrotomy for microscopic examination or to control bleeding. Only one of these (Case 5) had a happy result—well 3 years later. Case 15 gave no follow-up data. In Case 14, patient died of bleeding 4 weeks after excision of a polyp for hemorrhage. In Case 38, 50 polyps were removed by a diathermy snare through a gastrotomy, but many were left; death occurred 2 months later of general debility and liver insufficiency. Except for Case 38 no attempt was made in these to eradicate all the tumors but merely to stop bleeding or to obtain specimens for diagnosis.

It is thus apparent that the only safe method of treatment is the surgical removal of the tumor bearing area by gastric resection. The occurrence of malignant degeneration in this series in 19 of 37 cases giving malignancy data places gastric polyposis close to colonic polyposis in its tendency to malignant change and argues for wide removal. If the entire tumor bearing area cannot be amputated, as much of it should be resected as possible, and any tumors remaining in the stump should be excised and their bases thoroughly destroyed with cautery.

If the condition of the patient does not permit gastrectomy, and if there are only a few discrete polyps, the surgeon must compromise by excising the individual tumors and thoroughly destroying their bases. If there are a large number of polyps widely distributed over the mucosa, it is futile to attempt excision of only a few, except for diagnostic purposes. Bleeding should be controlled and the patient returned to bed. When he has been thoroughly prepared and his condition satisfactorily improved, a gastrectomy again should be attempted. If possible, the patient should not be subjected to surgery unless his condition warrants the performance of a gastric resection. Whole blood or plasma are often useful before and after operation. Gastroenterostomy is of no value.

If the differentiation of multiple gastric polyps into neoplastic and hyperplastic types is valid, the incidence of malignant degeneration may differ in the two types. From the microscopic descriptions in the reported cases it is not usually possible to make this differentiation. One would expect the congenital polyps to have a higher incidence of malignancy. For the time being, each case should be conducted in accordance with the total incidence of malignant degeneration. Further studies may allow us to alter our prognosis with the determination of the type of polyposis.

PROGNOSIS

In our previous report we found 12 per cent of cases malignant. Many of the cases in that series were reported long ago and the data were incomplete. In the present series of 41 cases 4 gave no malignancy data. Of the remaining 37, 19 were malignant. Statistics of other authors vary. Thus Lawrence found 18 per cent malignant degeneration in 50 autopsied cases of gastric polyps, over half of which were multiple. Stewart (106) found 28 per cent malignant degeneration in 47 cases, 20 of which were multiple; and Miller, Eliason, and Wright noted such changes in 20 per cent of 20 collected and personal cases.

The occurrence of malignant degeneration in over half of our present series argues for prompt and radical surgical measures. Fifteen patients were dead in from 1 day to 5 years after the institution of treatment. Gastric resection offers the best outlook and will eliminate the high incidence of malignancy if all the tumors are removed with the resected portion. In some cases the disease remains benign for many years, but each case should be treated by operation as soon as the diagnosis is reached and the patient satisfactorily prepared. Procrastination is useless and harmful. If malignancy has not yet supervened, gastric resection can produce an excellent result. If malignant invasion has occurred it is the most efficient method of treatment. The

Fig. 1.

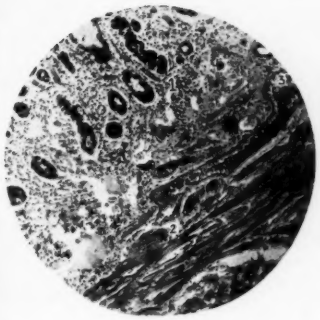

Fig. 2.

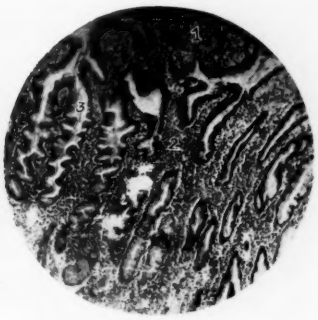

Fig. 3.

Fig. 1. Severe hypertrophic gastritis erroneously diagnosed "diffuse polyposis." The roentgenogram is "typical" of polyposis but operation showed a marked hypertrophic gastritis.

Fig. 2. Photomicrograph of specimen in case shown in Figure 1. Inner layer of mucous membrane. *1*, General edema and dilatation of capillaries; *2*, extension of infiltration among fibers of edematous muscularis mucosae; *3*, vessel containing large number of leucocytes.

Fig. 3. From same specimen as in Figure 2. Surface of mucous membrane. *1*, Edematous region; *2*, cellular infiltration; *3*, tortuous glands.

number of patients operated upon is too small and the period of observation too short to give reliable prognosis, but the gravity of the condition as a precursor of cancer is obvious.

REPORT OF PERSONAL CASES

CASE I. G. B., a male, aged 50 years, complained of intermittent attacks of constipation, flatulence, and bloody stools, occurring every 2 or 3 months, for the past 3 years. In the past year they were more frequent and severe. He had no nausea, vomiting or abdominal pain. There was slight soreness of the abdomen. He lost 4 pounds in the past 3 months. There were no serious past illnesses. He entered the hospital for study on January 3, 1938. Proctoscopic examination showed multiple growths of the descending colon. Two biopsy specimens were diagnosed by Dr. Rusk as "mucosal hyperplasia; no evidence of malignancy." A roentgenological examination of the large bowel showed multiple polyposis of the entire colon.

Since entry he had nausea and vomiting associated with distention which did not react to conservative measures. The stomach was kept empty with suction and the return water was always clear. Because of constant vomiting and distention an ileostomy was done on January 10, 1938, by H. B. Since that time he had had constant abdominal pain and vomiting. The vomitus contained gross blood. The suction was continued. On January 18, 1938, his temperature reached 39.6, degrees C.; leucocytes numbered 23,600 with 97 per cent polymorphonuclears. On January 21, 1938, a considerable amount of bright red blood was evacuated from the stomach through the tube. The tube was removed. The patient made a sudden exit.

At postmortem examination the following were noted: The stomach contained no blood. The cardia and upper fundal portion was studded with a large number of small, hemorrhagic polypoid growths, the largest only a few millimeters in diameter (Fig. 5). The gastric mucosa was ecchymotic in this region. There was a multiple polyposis of the entire colon from the cecum to the anus. Microscopic examina-

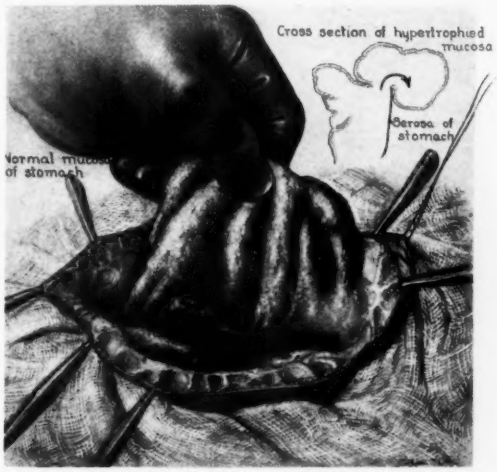

Fig. 4. Same case as in Figure 1. This shows the enormously hypertrophied folds of gastric mucosa as they are actually being withdrawn from the stomach through the gastrotomy incision. An area of hemorrhage and ulceration is shown.

Fig. 5. Case I. There are numerous small polyps principally in the cardiac and fundal portions of the stomach.

tion of the stomach showed the mucosa to be drawn into many small polypoid tumors. Most of the polyps were attached to the mucosa by a tiny stalk into which the muscularis mucosae, split into fine strands at the base, invaginated itself, while the submucosa followed into the stalk to a lesser extent. Varied was the degree of participation of the muscularis mucosae and especially of the submucosa in the formation of the stalk. The submucosa at times merely projected itself at the base of the polyp into a low, gradually arising peak, with only a small amount of its connective tissue taking part in the formation of the stalk (Fig. 6); in other instances it thrust itself well into the stalk, its connective tissue contributing to a greater or lesser extent to the groundwork of the tumor pattern (Fig. 7). The gastric glands in the region of the polyps showed little variation from the normal, except for some increase in the number of mucous cells. The stroma was normal except for slight edema. There was no noteworthy increase in lymphocytes or plasma cells. The gastric mucosa between the polypoid growths was normal. The colon showed the usual picture of multiple polyps with adenocarcinomatous degeneration on one polyp in the cecal region.

This patient came to autopsy without any thought in the mind of the attending physician of finding a pathological process in the stomach. All of the symptoms could have been explained on the basis of colonic polyposis with obstruction. The pathological picture in the stomach conformed more to the congenital type, but the epithelium was not neoplastic.

Case II. S. H., male, 78 years of age, entered the hospital April 6, 1935, complaining of pain in the chest of 10 years' duration. He had had syphilis in 1931 and received adequate antiluetic therapy. In January, 1931, he complained of pain in the epigastrium and vomiting whenever he ingested a heavy meal. Roentgenological examination showed a hernia of the fundus of the stomach through the esophageal hiatus of the diaphragm. This was held to account for his gastric symptoms.

Examination showed a typical cardiac insufficiency with decompensation and marked dependent edema. Blood pressure was 190/70. Blood and spinal fluid Wassermann were negative. There was no edema. He expired suddenly.

At postmortem examination the following findings were noted: The mucosa of the stomach was found to bear 111 polypoid masses varying from ½ to 3 centimeters in diameter diffusely scattered, but mainly grouped along the lesser curvature and pylorus (Figs. 8 and 9). All were pedunculated and had thin stalks. Some of the polyps showed superficial necrosis. There were no polyps in the small intestine but there were 6 similar polyps in the cecum. There was no gross evidence of malignancy.

Microscopic sections of the stomach (Figs. 10 and 11) showed the polyps to be composed of tall columnar epithelium arranged in acini around a central core. Some of the acini were greatly dilated and contained faintly stained pink material. The epithelium showed some hyperplasia but the cells were not markedly altered and there was no evidence of malignant degeneration. The transition of the mucosa from the normal to that described was very gradual. At the attachments of the polyps to the mucosa, the muscularis mucosae was split and its fibers carried into the stalk, often into the tumor itself; the submucosa, too, followed the muscularis mucosae, its connective tissue entering the stalk and forming in part the stroma of the tumor. Occasional lymphocytes were seen in the stalk. Sections from the colon showed a small polyp composed of rather uniform small acini lined by tall columnar epithelium which was distinctly piled up in places and contained occasional mitotic figures. The stroma was compact and had numerous lymphocytes plasma cells and eosinophiles. There was no evidence of malignancy.

The presence of gastric symptoms of 7 years' duration were amply accounted for by the hernia of the fundus of the stomach through the diaphragm. From the clinical standpoint the discovery of multiple gastric

Fig. 6. Case I. Sections through the stomach show the small polypoid tumors arising from the mucosa. In this section the muscularis mucosae tends merely to dip into the stalk and does not enter the tumor. The submucosa plays little or no part in the formation of the polyp. The epithelium shows little variation from the normal.

Fig. 7. Case I. The muscularis mucosae and the submucosa enter the stalk for a greater distance than in the previous figure. Here the muscularis mucosae and the submucosa insinuate themselves into the stalk and contribute to the formation of the groundwork of the tumor.

polyposis in the autopsied stomach was a surprise. The x-ray films previously taken in 1931 were again inspected. The ectopic position of the fundus was noted, but the roentgenologist had completely overlooked filling defects characteristic of polyps in the herniated portion. The error in not discovering these lesions before death, is therefore, an oversight on the part of the roentgenologist. The case falls into the class of congenital polyps.

Case III. B. S., a retired salesman of 74 years entered Mt. Zion Hospital May 23, 1940. He was well until 6 weeks ago when he developed vomiting following the ingestion of solid foods. This usually occurred several hours after eating. The condition became steadily worse so that during the past 2 weeks he could only retain eggs and liquids. He regurgitated his food at night. This was never sour or bitter. The vomitus occasionally was streaked with fresh blood. He had no abdominal pain. His stools were not bloody or tarry. He had been subject to chronic constipation for years. Since the onset of his illness he lost 15 pounds in weight. He smoked moderately, used no alcohol.

On physical examination one found an avoid mass in the epigastrium about 6 centimeters in diameter, nontender, smooth, and movable. A smooth liver edge was felt 3 centimeters below the costal margin. His blood pressure was 90/60. There were no other abnormal physical findings.

Roentgenological examination May 15, 1940, at Stanford Hospital showed 90 per cent retention in 5 hours. The stomach was large, containing much fluid and particles of food material. At the pylorus was felt a tumor which constricted the lumen considerably and left the wall stiff. Vigorous peristaltic waves ran down to this area and stopped promptly. The roentgenological diagnosis was "carcinoma of the stomach."

Gastroscopy was performed by Dr. Allan Cohn on May 29, 1940, with the following report: The entire antrum is involved in a diffuse carcinomatous nodular process with a polypoid excrescence. The body of the stomach is similarly involved by a diffuse nodular process, with a polypoid excrescence presenting from the lesser curvature. The changes extend well into the upper third of the stomach, but the tumor edge cannot be well seen because of a mucous lake.

Impression: Diffusely infiltrating carcinoma.

Laboratory investigation revealed the following positive findings: urine—albumin, very slight trace; sugar, negative; leucocytes, 3–5 per high dry field; erythrocytes–30–50 per high dry field. Blood—hemoglobin 10.8 grams; red blood cells, 4,100,000; white blood cells, 6,600; differential count, normal. Stool—occult blood moderately positive. Blood Wassermann—negative. Gastric analysis (alcohol meal) showed:

	F.C.	1	2
Cubic centimeter	40	80	60
Free hydrochloric acid	0	0	0
Total hydrochloric acid	10	5	5

The clinical diagnosis was carcinoma of the stomach. Operation was performed by Dr. F. I. Harris on May 31, 1940. Exploration revealed a nodular tumor occupying the pyloric end of the stomach. Several enlarged lymph nodes were felt in the lesser omentum. The liver was normal. A subtotal gastric resection of the Hoffmeister-Finsterer type was performed. The involvement of the neoplasm was so extensive that the line of resection was through the tumor and part of the growth was left *in situ*. The postoperative diagnosis was "gastric carcinoma with metastases to the lesser omentum and retroperitonea

Fig. 8. Case II. Many pedunculated polyps are seen diffusely scattered over the gastric mucosa, but especially numerous over the mucosa of the lower third of the stomach. One hundred eleven polyps were counted. The mucosa between the tumors appears normal.

lymph nodes." The patient died on the 5th day after operation with jaundice, peritonitis, and terminal pneumonia.

In the specimen, multiple large nodes were felt through the serosa on the anterior and posterior walls; one large firm mass was felt in the antrum.

Fig. 10. Case II. A pedunculated polyp showing the muscularis mucosae and the submucosa entering the stalk and forming the groundwork of the tumor pattern. Dilated gastric glands are visible.

Fig. 9. Case II. The lower third of the stomach showing the polypoid growths separated by apparently normal mucosa.

When the specimen was opened a large stenosing, ulcerated carcinoma involving almost the entire antrum was found. Most of the remainder of the stomach was covered with a large number of soft polypoid excrescences, some as much as 2 centimeters high (Fig. 12). From 3 to 6 centimeters of normal appearing mucosa separated the area of multiple polyposis from the carcinoma. The resection was through an area of multiple polyposis.

Microscopic examination of the stomach (Figs. 13, 14) showed the muscularis thick and hypertrophied. In the submucosa were several focal accumulations

Fig. 11. Case II. The gastric glands are dilated. The glandular epithelium shows some hyperplasia but the cells are not markedly altered.

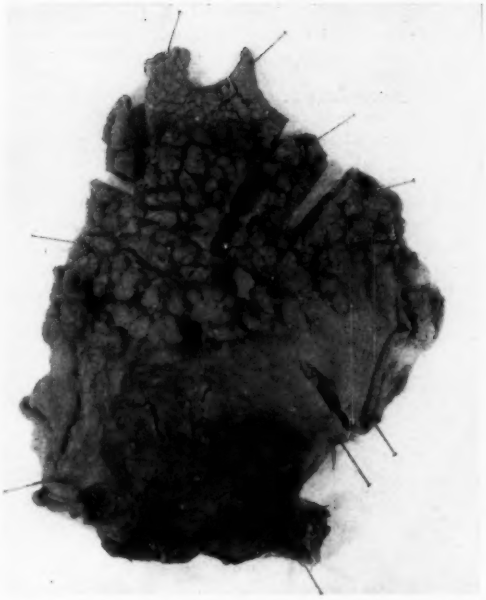

Fig. 12. Case III. A large number of closely placed polyps are seen in the cardia and upper fundal portion of the gastric mucosa. In the pyloric portion is a large ulcerating carcinoma. A strip of normal appearing mucosa separates the carcinomatous area from the area bearing the polyps.

of plasma cells and lymphocytes with a few scattered polymorphonuclear leucocytes. The polyps were composed of a thick layer of rather hypertrophic gastric mucosa arranged about a central core. The cells lining the glands were tall and had an abundance of clear cytoplasm of the mucous type. They showed no striking variation from the normal. At the area of attachment of the polyp, the muscularis mucosae was split and its fibers entered the growth, its connective tissue contributing to the formation of the core. In many places the polyps branched. There was no evidence of malignant alteration. Three similar polyps were found in the colon; 1 in the bladder.

The diagnosis of the clinician, the roentgenologist and the gastroscopist before operation, and the surgeon at operation was carcinoma. The specimen showed the carcinoma, but in addition a widespread multiple gastric polyposis with individual tumors projecting into the lumen as far as 2 centimeters. It is true that at gastroscopy two polypoid growths were noted by Dr. A. Cohn; but the essentially diffuse and multiple character of the benign lesion was not even then recognized. The

Fig. 13. Case III. The muscularis mucosae is split and its fibers enter the tumor. The submucosa follows the muscularis mucosae partly to form the stroma of the tumor.

microscopic picture showed the tumors to conform to the congenital type.

Case IV. Chronic hypertrophic gastritis erroneously diagnosed polyposis or polypoid malignancy. J. L., a sheep raiser, aged 46 years, complained of attacks of nausea and blood-streaked vomiting. He was constipated for years. On July 18, 1938, following a light lunch, he started to vomit and had been vomiting daily since that time. He often retched and developed a severe cramping pain in the lower abdomen. At the end of a period of retching there would be a few streaks of blood in the vomitus but at no time did he have a massive hemorrhage. In the past few weeks he had been vomiting almost constantly. On physical examination there was a def-

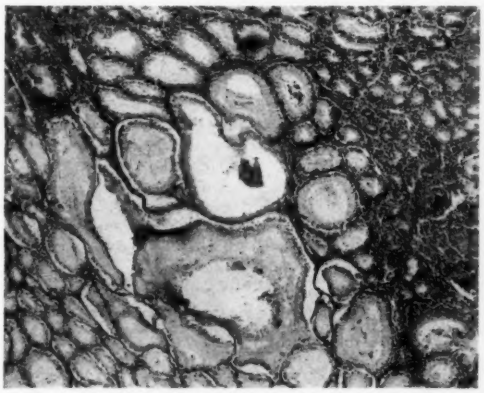

Fig. 14. Case III. Many of the gastric glands are dilated. Often the epithelial cells contain an abundance of clear cytoplasm suggesting the presence of mucus. The epithelium shows no striking change from the normal.

Fig. 15. Case IV. "Nodular mottling of the lower two-thirds of the stomach outline producing the appearance of an irregular polypoid carcinoma." The roentgenological diagnosis was "polypoid tumor of the stomach"; the roentgenologist felt that the lesion was extensive, probably inoperable, a true polyposis or an unusual sarcoma. Two weeks after x-ray therapy, re-examination showed irregular defects extending to the cardia.

inite area of tenderness in the midepigastrium. There were no masses and no rigidity. His hemoglobin was 80 per cent, erythrocytes, 4,000,000; blood Wassermann and urine were negative. He lost 15 pounds in the past 3 weeks. Patient refused gastric analysis but the vomitus showed an absence of free hydrochloric acid, and a total of only 7; there was a positive test for occult blood. The stool showed a positive test for occult blood on two occasions. Roentgenological examination showed a nodular mottling of the lower two-thirds of the stomach outline producing the appearance of an irregular polypoid carcinoma (Fig. 15). The roentgenological diagnosis was "polypoid tumor of the stomach." The roentgenologist was of the opinion that the lesion was extensive, probably inoperable; a true polyposis or an unusual sarcoma.

The patient was given a course of x-ray therapy. Re-examination 2 weeks later showed multiple irregular nodular defects extending from the pylorus well up to the cardia. The appearance was that of a rather diffuse papillomatous new-growth. In view of the failure of the lesion to respond to radiation, surgery was advised.

Operation was performed on September 7, 1938. The abdomen was opened by one of us (H. B.). Nothing abnormal could be felt in the stomach or duodenum except a slight thickening of the gastric wall. There was no induration, no enlarged glands. The spleen, liver, pancreas, and gall bladder were normal. Anterior gastrotomy revealed that the mucous membrane was thrown into high thickened folds with deep sulci between them. Most of these ridges ran longitudinally but one fold about one-half inch wide ran obliquely posteriorly. There was no sign of a polypoid tumor anywhere in the stomach. The ridges were from 1 to ½ centimeter in height and had a normal pink color before manipulation. Here and there in the sulci there were small, round, soft, circumscribed reddish areas about 4 millimeters in diameter which were probably areas of gastritis. Except for this the sulci were a pale pink. A large amount of mucus covered the entire mucosal surface of the stomach. The ridges were highest in the pylorus and midportion to the stomach, gradually becoming thinner and lower as the cardia was reached. There was no bleeding from the mucosa.

It was impossible to make a definite diagnosis at the time of operation but, in view of the history and other findings, a subtotal gastrectomy was done. Inspection of the cardiac stump showed that the mucous membrane was found to be moderately hypertrophic with some prolapsing of the mucosa of the anterior wall. There were no polypoid tumors. About 1 inch of the anterior wall of the gastric stump, which contained the hypertrophic mucous membrane, was removed in addition to the part of the stomach previously resected. The patient made an uninterrupted recovery.

Examination of surgical specimen. Figure 17 is a drawing of the specimen and gives a good idea of the

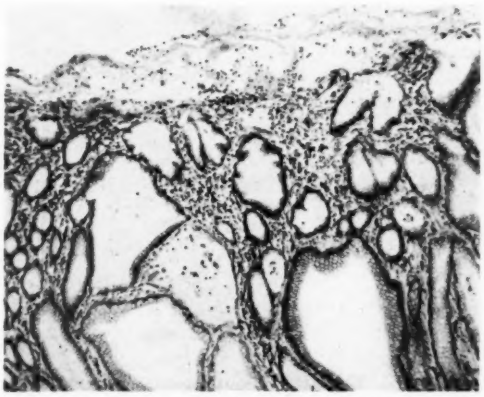

Fig. 16. Case IV. Chronic hypertrophic gastritis. The glands are tortuous, some are branching. Many are dilated, forming cysts, some of which contain plasma cells and red blood cells. In the interstices between the crypts are plasma cells, eosinophils, and lymphocytes. The epithelial cells are often high and cylindrical, containing considerable mucus; those lining some of the cysts are flattened. The mucosal surface is covered with a layer resembling fibrin.

Fig. 17. Case IV. Hypertrophic gastritis erroneously diagnosed as polyposis or polypoid malignancy.

gross pathology. In short, the resected portion of the stomach showed a marked hypertrophy of the mucous membrane which was thrown into large folds. The description of the stomach at operation was exactly the same as that found in the resected portion.

The photomicrograph, Figure 16, reveals evidence of a chronic hypertrophic gastritis of severe grade without any evidence of papilloma formation. The detailed report of microscopic examination follows:

In many portions of all sections the surface epithelium is missing. The pits are extraordinarily elongated, partly corkscrew-like, branching and showing cystic enlargement in quite a few areas. The epithelium of the crypts is cylindrical and high. However, some of the cysts have a very flat, compressed epithelium. In the interior of the cysts many plasma cells and red blood cells are seen. The interstices between the elongated pits contain plasma cells and eosinophils. The body glands are normal, but at some places the cysts are so large as almost to reach the muscularis mucosae and to replace the body glands entirely. There is slight infiltration in the submucosa but not in the muscularis. Some lymph follicles penetrate through the muscularis into the submucosa. Extensive hemorrhage seen in the submucosa may be artificial. However, in slide 3 the superficial capillaries are enlarged and in one place the cystically enlarged pits are covered with blood at the surface, which does not seem to be an artefact as signs of organization (strands of fibrin) are visible.

Microscopic diagnosis: severe proliferative, cystic hemorrhagic chronic gastritis.

The history and x-rays findings in this case were considered diagnostic of an intrinsic lesion of the stomach probably either a polyposis or a polypoid malignancy. To the surprise of everyone a marked hypertrophic gastritis was found in the resected stomach. This case is very similar to a case previously reported by Brunn and Pearl in which the same error was made. In both cases polypoid lesions were diagnosed but the pathological lesion proved to be chronic hypertrophic gastritis.

SUMMARY

This report is an analysis of 41 cases of gastric polyposis having 3 or more polyps, in-

TABLE III.—CASE DATA

Case, date reported, age and sex	Author	Method of making correct diagnosis	Excessive alcohol	Hereditary polyposis	Duration	Symptoms								Physical signs			Gastric analysis						X-ray	Treatment
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Hematemesis	Weakness	Constipation	Tumor	Tenderness	Rigidity	Free HCl	Total HCl	Ferments	Blood	Tumor tissue	Mysorrhea		
1 1927 69 M	Cameron and Wright-Smith	P.M.			2 mos.	+	+	○	○	+	+	+	+	+	+	○							Delay in emptying. No intrinsic lesion	Medical
2 1928 48 M	Mason and Dwyer	Operation			25 yrs.					+													One year ago normal. Now three tumors	Gastrotomy. Excision of polyps
3 1928 33 F	Strauss, Meyer and Bloom	Operation			9 yrs.	+ *		+			+			○	+		○ ○	22 17		+		+ †	No retention. Characteristic polyposis of cardia	Subtotal gastrectomy
4 1928 38 M	Strauss, Meyer and Bloom	Operation			2 yrs.	+								○	○	○	○			○			Serrated pylorus; defective duodenal bulb	Gastric resection
5 1928 50 M	Lamas	Operation			2 mos.	+									+								Ulcer niche on lesser curvature	Gastrotomy. Biopsy
6 1929 58 M	Lamas and Fuentes	Operation	○		5 mos.		+	+					+		○	○	○			○			Single defect in pylorus	Gastrotomy. Biopsy
7 1930 58 F	Ackman	X-ray			5 yrs.						+	+		+			○	18		○		+ †	Filling defect upper third greater curvature and pylorus. Defective duodenal cap. suggestive of prolapsed polypi	Partial gastrectomy and duodenectomy
8 1930 48 M	Miller, Eliason-Wright	Operation			10 yrs.	+			○	○				○			○						Nodular defect in antrum	Gastrotomy. Excision of polyps
9 1930 61 F	Miller, Eliason-Wright	Surgical specimen			6 yrs.	+	+	○	○	+					+		○	25		+			Lesion of greater curvature, marked residue; hyperperistalsis	Gastric resection
10 1931 55 M	Kment	X-ray			6 wks.	+	+	+	+								○	14					3–4 filling defects in pars media	Gastrotomy. Removal of polyps
11 1931 33 M	Kment	X-ray			9 yrs.	+	+ *	+	+								○	9					2 filling defects. Good peristalsis	Billroth I resection

*Stomach trouble 9 yrs. †In spec.

TABLE III.—CASE DATA

Course	Part involved: Upper ⅓	Middle ⅓	Lower ⅓	Greater curvature	Lesser curvature	Anterior wall	Posterior wall	Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood-stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
Death in 2 days from hematemesis				+		+		18	*Polyadenome polypeaux*	None	−					O	O	O	Vague indigestion 35 years ago —for 3 years abdomen very distended. Jaundiced for 6 wks. At p.m. 4,000 c.c. bile-stained ascites. Large amount old and recent blood in stomach. Gastric mucosa atrophic, but wall hypertrophied. Carcinoma of pancreas with pulmonary metastases
No diarrhea since operation	+	+					+	5	Benign polyps	Polyps			O		+		O	O	Presenting symptom — diarrhea of 25 yrs. standing. 3 tumors on x-ray, 5 at operation
No relief from Sippy regimen before operation. Uneventful convalescence after operation	+	+	+	+		+	+	Numerous	*Polyadenome en nappe*	Intrinsic gastric lesion, probably malignant		O		−	+	O	O		Markedly hypertrophic mucosal rugae, at times 5 cm. deep. Onset with sudden pain and hematemesis
Blood picture 10 months after operation resembled pernicious anemia	+	+	+					Numerous	*Polyadenome en nappe.* Hypertrophy gastric glands	None		*	O			+	O		No clinical diagnosis in report
Well 3 yrs. after operation	+	+	+	+	+	+	+	Many	Adenomatous polyp with probable malignant degeneration	Ulcer						+	+†		Entire gastric mucosa covered with vegetations. Resection impossible. At operation stomach normal on first examination
5 mos. after operation dizziness and heart trouble; transient jaundice	+		+	+	+	+		3	Adenocarcinoma	Gastric tumor	−	O		−			+		Resection impossible. Tumors missed by barium meal were found by pneumogastrography. X-ray showed pyloric polyp; overlooked 2 polyps in upper stomach
No symptoms 1 yr. after operation	+	+	+	+	+	+		9	Multiple adenopapillomas (*en nappe*). carcinoma	Papillomas of stomach and duodenum, with malignancy		‡			10	+	+§		Initial symptom severe gastric hemorrhage. Polypoid mass prolapsed into duodenum without obstruction. Liver enlarged. Blood pressure 260/111. Toxic adenoma of thyroid
3 mos. after operation recurrence of pain; x-rays negative, still no free HCl			+				+	3	Polyps, carcinoma	Polyp or carcinoma		O		−	30		+		Diagnosed carcinoma of stomach in 1917. Stomach and duodenum normal at operation in 1920—appendectomy performed. Achlorhydria 1920–1926. No anemia
3 mos. after operation slight gastric residue; 6 mos. after, weight gain 20 lbs.; 1 yr. after, mass in left lower quadrant; enlarged liver; (?) malignancy		+	+	+	+			3	Adenoma and adenocarcinoma	Probable carcinoma			+	−	25		+	¶	Diarrhea presenting symptom. Increased mucus in stool
Death 2 days after operation from peritonitis		+						10	Adenomatous polyps	Polyp or carcinoma			+				O	¶	4 defects by x-ray; 10 tumors at operation
		+	+		+	+		4	Polyps. No malignancy	Polyps. No malignancy			**		26	+	O		2 defects by x-ray; 4 tumors at operation

*Severe-like pernicious anemia †Probable ‡Moderate §In large polyp ¶Small rectal polyp **Melena

TABLE III.—CASE DATA—Continued

Case, date reported, age and sex	Author	Method of making correct diagnosis	Excessive alcohol	Hereditary polyposis	Duration	Symptoms								Physical signs			Gastric analysis						X-ray	Treatment
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Hematemesis	Weakness	Constipation	Tumor	Tenderness	Rigidity	Free HCl	Total HCl	Ferments	Blood	Tumor tissue	Mixorrhea		
12 1931 33 F	Kment	X-ray			2½ mos.	O	O	O	O	O	O	+	O				O	6					Several pedunculated tumors in pars media	Gastric resection
13 1931 54 M	Kment	X-ray			1 yr.	+											O	4					2 filling defects	Excision of 5 polyps
14 1931 56 M	Kment	X-ray			2 mos.	+	+					+					O	16					Many defects entire stomach	Gastrotomy. Excision of some polyps to stop bleeding
15 1932 23 M	Becchini	Operation			1 yr.	+			+													+ *	Many irregular defects	Biopsy
16 1932 51 F	Habbe	X-ray		O	8 mos.	O	+		+		O			O	O	O	O	12		O			Many defects in stomach and duodenum. 40% retention	Removal one polyp. Gastrojejunostomy
17 1932 47 F	Neuman	Operation			1 yr.							+											Multiple filling defects	Gastrotomy. Excision of polyps
18 1932 52 M	Palonskier	P.M.		O	6 mos.	O	O	+	O	O	O	O	O											
19 1933 48 M	Kirchow	P.M.	+		?	O	O	O	O			+			+	O								Medical. No operation
20 1933 57 F	Sinclair	Surgical specimen	O		14 yrs.	+	O		+	+							O †					+ ‡	Hour-glass deformity	Resection ⅔ of stomach
21 1934 47 M	Benedict and Allen	Operation			6 mos.	+			+		+	+		+			O §			+			Large mottled filling defect; 5 yrs. later(?) multiple polypoid masses	Excision of 5 tumors
22 1934 49 M	Benedict and Allen	P.M.			1½ yrs.	+		O	O								O						Large defect on posterior wall of upper third and middle third	Medical, no operation
23 1934 58 M	Benedict and Allen	X-ray			6 mos.	+						+						5 ¶					Multiple defects on greater curvature	Subtotal gastrectomy. Cautery excision of one polyp in gastric stump
24 1934 35 M	Ochlecker	X-ray			15 yrs.	+			+														Many filling defects	Subtotal resection. Excision small no. polyps in gastric stump. X-ray therapy before operation

*In spec. †4 weeks after operation ‡In vomitus §5 years after operation ¶(alc)

TABLE III.—CASE DATA—Continued

Course	Part involved: Upper ⅓	Middle ⅓	Lower ⅓	Greater curvature	Lesser curvature	Anterior wall	Posterior wall	Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood-stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
Death 3 days after operation from anemia	+	+						Many	Polyposis. Medullary carcinoma	Possible malignancy		*	+				+		No gastric symptoms
Death 1 day after operation from pulmonary edema		+	+			+		5	Polyposis. Papillary carcinoma. Pernicious anemia	Benign polyps			†		33		+		Blood picture like pernicious anemia. Slight icterus, 4 mos. duration; paresthesia of extremities. 2 filling defects on x-ray; 5 tumors in stomach at operation
Death 4 wks. after operation from hemorrhage despite repeated transfusions	+	+	+	+	+	+	+	Many	Papillomas; adenocarcinoma	Polyposis		+	+		‡		+		Severe anemia. Malignancy not demonstrated in surgical specimen but definite at autopsy
	+	+	+	+	+	+	+	Many	*Polyadenome en nappe.* Chronic gastritis	Diffuse infiltration gastric wall probably benign						+	○		Resection not possible. Definite invasion of submucosa, but no atypical abnormal staining or mitosis
Death 4 days later of cerebral embolism; (?) ileus or acute dilatation of stomach		+	+					Many	Polyposis with malignancy	Carcinoma of stomach or esophagus	+,+ §	+	+		40		+		Duodenal involvement questionable
Gained 16 lbs. 6 wks. after operation							+	5	Benign polyps	Carcinoma		+	†		+		○		Too weak to stand gastric resection
Death. No operation	+	+	+	+	+	+		7	Polyps (inflammatory hyperplasias)	None antemortem						+	○		Atrophic—hypertrophic gastritis of entire mucosa
Delirium and death 5 days; (?) alcoholism	+			+				3	Polyposis with malignancy	None			+			+	+		Malignancy in one polyp only. Alcoholic hallucinosis; cachexia
Completely relieved of symptoms	+	+	+	+	+	+	+	Many. 40 polyps per sq. in.	Polyposis	Hour-glass stomach		○		−	+	+*	○	○	Almost complete obstruction of pylorus by polypi
Relieved for 5 yrs. Then re-operation for polypoid masses. Death from peritonitis	+	+	+	+			+	First operation—5; 2nd, many	Polyposis. Adenocarcinoma	Probable malignancy		+	+		15		+		Condition did not warrant resection of stomach at 2d operation
Death after 33 days	+	+	+	+	+	+	+	group	Polyps. Adenocarcinoma	Carcinoma					20		+	○	Blood culture positive for Streptococcus-viridans, 2 carcinomas probably developing from benign tumors
No symptoms 7 mos. after operation	+	+	+	+	+	+	+	Over 100	Adenomatous polyps	Polyposis		+	+		30	+	○		Frozen section of 3 polyps at operation
Relief	+	+	+	+	+	+	+	Many	Polyposis with malignancy	Fibrosarcoma or benign polyposis		○			○		+	○	Carcinoma in one area. Metastatic gland in lesser omentum

*Severe †Melena ‡Marked §Alb.

TABLE III.—CASE DATA—Continued

Case, date reported, age and sex	Author	Method of making correct diagnosis	Excessive alcohol	Hereditary polyposis	Duration	Symptoms								Physical signs			Gastric analysis						X-ray	Treatment
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Hematemesis	Weakness	Constipation	Tumor	Tenderness	Rigidity	Free HCl	Total HCl	Ferments	Blood	Tumor tissue	Mycorrhea		
25 1935 53 M	McRoberts	X-ray			5 yrs.	−			○					○	○	○	○	4					3 polyps on posterior wall	Pólya resection
26 1935 58 M	McRoberts	Surgical specimen			1 mo.	+	○	○	○	○	−	+											Duodenal ulcer	Partial gastrectomy and duodenectomy
27 1935 40 M	McRoberts	Surgical specimen			15 yrs.	+	*					+			+		S	18					No ulcers	Pólya partial gastrectomy
28 1935 42 M	McRoberts	Operation			10 yrs.	−	+	−	−		○	+			−		1926 0	1926 S		+ †			1926 carcinoma lower ⅓ of body of stomach	1926 cautery excision of polyps
																	1929 0						1929—negative	
																	1933 0	1933 14					1933 polypoid carcinoma of mid-stomach	1933 exploratory; biopsy of extragastric gland
29 1935 52 M	Ravenswaay	X-ray			5 yrs.	+			○	○			+	+	+		○			+			Multiple filling defects	Complete gastrectomy
30 1935 49 F	Pendergrass and Andrews	X-ray			(?)	○ *	○	○	○		○						S to 20	10 to 60					Slight 7 hr. residue. Central filling defect of pyloric canal. Other small defects	Gastrotomy. Excision of polyps. Pyloroplasty
31 1936 50 M	Van Buskirk	X-ray			1 yr.	−			−		−						○	25					Multiple polyps	Gastrojejunostomy
32 1936 42 M	Van Buskirk	X-ray			(?)	+			−		−			+			§	§					Multiple defects entire stomach and first part of duodenum	
33 1936 52 M	Poerkel	X-ray			5 yrs.	−	○	○	○	○			○	○	○	○							Multiple filling defects in antrum and duodenal bulb	Gastric resection (Pólya)
34 1936 45 M	Popovic	X-ray			(?)	−	○		○	−			○	○			○	4					Multiple filling defects; mucous membrane thickened	Billroth II resection of stomach
35 1937 45 F	Holman	Operation			1 wk.	−								+	+	+								Resection of stomach and first part of duodenum
36 1937 50 F	Hunt	X-ray			13 yrs.	−																	Multiple gastric polyps	Sleeve resection of stomach. Local excision of 3 polyps in cardiac stump

*Ulcer symptoms. †Trace ‡No gastric complaints §Not done

TABLE III.—CASE DATA—Continued

Course	Part involved: Upper ⅓	Middle ⅓	Lower ⅓	Greater curvature	Lesser curvature	Anterior wall	Posterior wall	Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood-stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
		+	+				+	Many	Adenomatous polyps	Polyps			○				○		
		+						Multiple	Gastric ulcer. Polyposis	Duodenal ulcer		+	+*			+			Gastric resection for ulcer. Polyps found in surgical specimen in addition to ulcer
			+					Multiple	Multiple sessile polyps. Chronic gastritis	Ulcer		+†				+			Gastroenterostomy for multiple ulcers 15 yrs. ago; cautery excision high gastric ulcer and cholecystectomy 14 yrs. ago; relief for 5 yrs. then ulcer symptoms
1926–1931—no symptoms. Then recurrence of pain, weakness and melena. 1933—large carcinoma		+	+				+	3	Polyps. "Carcinoma *in situ*"	Carcinoma		+	‡		17		+		No metastases in excised gland in 1926. In 1933, inoperable carcinoma with metastases to extragastric gland
Death 12 hrs. after operation (pneumonia)	+	+	+	+	+	+	+	Large number	Benign polyposis	Diffuse polyposis		§	○		20	○	○		Spleen removed on account of bleeding. At p.m. stomach distended with blood
Death 1 year after operation			+					Several	Polyps	Multiple prolapsing polyps				–	18				Stomach negative to palpation at operation. Polyps attached to redundant gastric mucosa found on gastrotomy
	+	+	+	+	+	+	+	Many	No specimen	Multiple polyposis									Vomited 2 tumors on one occasion. Stomach wall covered with many small polyps
Well for 1 yr. Then return of symptoms and large palpable mass. Died 2 yrs. after operation of carcinomatosis	+	+	+	+	+	+	+	Many	No specimen	Multiple polyposis							+		Entire stomach and first part duodenum covered with polyps. (Note duodenal involvement.) (See text.)
Well 4 yrs. after operation. X-rays repeatedly negative			+				+	Multiple	Adenocarcinoma. Multiple polyps	Prolapsed gastric polyps with probable malignancy	–	§		–			+		Polyps prolapsed into duodenum
Complicating subphrenic abscess. Death in 2 wks.				+				Several	Polyposis ventriculi circumscripta	Polypoid carcinoma	¶		○	–			○		Multiple degenerative processes in central nervous system
Well 15 mos. after operation	+	+	+	+	+	+	+	Multiple	Polyposis. Hypertrophic gastritis. Duodenitis	Surgical abdomen							○		Operation for acute perforation of duodenal ulcer. Stomach filled with polyps. Specimen shows polypoid folds up to 1 inch thick, abruptly ending at duodenum. Inflammation of duodenum
	+	+					+	Several	Polyposis with malignancy	Multiple gastric polyps	–		+**		+††		+		Diagnosed pernicious anemia

*Large tarry stools †Mild ‡Melena, tarry stools §Slight ¶Albumin trace **Constant ††Marked

TABLE III.—CASE DATA—Continued

Case, date reported, age and sex	Author	Method of making correct diagnosis	Excessive alcohol	Hereditary polyposis	Duration	Symptoms								Physical signs			Gastric analysis						X-ray	Treatment
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Hematemesis	Weakness	Constipation	Tumor	Tenderness	Rigidity	Free HCl	Total HCl	Ferments	Blood	Tumor tissue	Myxorrhea		
37 1937 55 M	Christopher	Operation			1 yr.	+	O	O	O	O	O	O	+	O	O	O	O						"Large carcinoma of body"	Gastrotomy. Subtotal Pólya resection
38 1940 29* F	Glass	Operation	O		9 yrs.	+‡	+	+	+	O	O	+	+	O	O	O							No report	Snare excision through gastrostomy
39 1942 50 M	Pearl and Brunn	P.M.	O	O	3 yrs.	+		+	+	O	O		+	O	O	O							No x-ray of stomach; diffuse polyposis of colon	Ileostomy for vomiting and distention
40 1942 78 M	Pearl and Brunn	P.M.	O	O	4 yrs.	+			+														1931—Diaphragmatic hernia. Normal stomach	No treatment for gastric symptoms
41 1942 74 M	Pearl and Brunn	Surgical specimen	O	O	6 wks.	O	O	+	+	O	+	+	+	+	O	O	O	10			O	O	90% retention; stomach contained food and fluid; constricting lesion at pylorus. Diagnosis: carcinoma of stomach	Subtotal gastric resection

*Age gastric polyps discovered ‡Digestive symptom since 1910 at age 12 years

cluding 3 new personal cases. It is supplementary to a previous report of 84 cases published by Brunn and Pearl in 1926.

Multiple gastric polyposis may be congenital (neoplastic) or inflammatory (hyperplastic). The two types may often be differentiated on gross examination alone. On microscopic examination one finds that in neoplastic polyps the muscularis mucosae enters the tumor for a variable distance and usually becomes fragmented or split, with the submucosa entering the tumor for a variable extent. In the hyperplastic types the muscularis mucosae is intact and forms a delineating membrane, the submucosa playing no part in the formation of the tumor. Borderline cases may be difficult to classify.

The symptoms are not characteristic. In the series, epigastric pain and tenderness were most frequent. In over half of the cases,

TABLE III.—CASE DATA—Continued

Course	Part involved: Upper ⅓	Middle ⅓	Lower ⅓	Greater curvature	Lesser curvature	Anterior wall	Posterior wall	Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult Blood-stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
10 lbs. increase in weight 4 mos. later	+	+	+	+	+	+	+		Diffuse adenocarcinomatous metaplasia. *Polyadenome en nappe*	Carcinoma of stomach	−			−	12	+	+	○	Unusually diffuse carcinomatous involvement
Death from "liver" after 9 operations for polyps and their complications	+	+	+	+	+	+	+	Many	Gastrointestinal polyposis	Gastrointestinal polyposis		*			†		○	+	In 1918, at age 20, excision 4 duodenal polyps and gastroenterostomy for pain, and severe bleeding diagnosed as "duodenal ulcer and amebic dysentery." In 1919 resection 3 feet of ileum for intussusception; 3 polyps in specimen. In 1928, second intussusception not requiring resection; opened ileum showed 5 polyps which were excised. In 1929, fulguration rectosigmoid polyps; 1 mo. later large polyp removed from cecum was diagnosed adenocarcinoma. In 1930, anastomosis transverse colon to sigmoid and left colectomy. In 1937, operation for pyloric obstruction showed multiple polyposis entire stomach; too ill for gastric resection. Endotherm snare excision numerous polyps through Janeway gastrostomy. "Liver" death.
Death 10 days after operation from peritonitis	+							Many	Polyposis of stomach and colon	Polyposis of colon			+		4		○	+	Fresh blood recovered from stomach tube treating intestinal obstruction
Death from cardiac failure	+	+	+	+	+	+	+	50–100	Polyposis of stomach and large bowel	Diaphragmatic hernia of stomach		○		−			○	+	Syphilitic history but blood Wassermann and cerebrospinal fluid negative. Polyposis diagnosed in retrospect examination of films
Death 5 days after operation with jaundice, peritonitis and terminal pneumonia	+	+	+	+	+	+	+	Large number—over 100	Diffuse polyposis with adenocarcinoma of antrum	Carcinoma	‡§	Sl.	+	−	15	+	+	+¶	Gastroscopy showed "polypoid excrescence" in antrum and in body; diffuse nodular process of body; impression — "diffusely infiltrating carcinoma." The essentially diffuse nature of the multiple polyposis was not noted on gastroscopy

*Hb 38% in 1918 †Marked ‡Albumin trace §40 RBC N. D. F. ¶Colon, bladder

bleeding was found to take place in the vomitus, stool, or gastric content. Pedunculated tumors and those near the pylorus are more apt to give symptoms of separation of polyps or pyloric obstruction. Some patients have had symptoms over 20 years. The physical findings are indefinite and may be entirely lacking.

The diagnosis is attended with considerable difficulty. The x-ray may fail to differentiate multiple polyposis from chronic hypertrophic gastritis, retained food, bezoar, or sarcoma. The correct diagnosis was made most often by x-ray and by operation, but the condition was often overlooked by the roentgenologist. Gastroscopy is a valuable aid in the diagnosis of gastropathies, especially in the differentiation between benign and malignant lesions, and between polyposis and hypertrophic gastritis. Both methods are complementary and their

combined use will greatly enhance our diagnostic acumen.

Free hydrochloric acid was absent from the fasting gastric content in almost every case. Careful search should be made in the gastric content for tumor particles which may establish the diagnosis.

In our previous series malignant alteration was noted in 12 per cent. Of the present series of 41 collected and personal cases since 1926, 4 gave no malignancy data. Of the remaining 37, malignant alteration was found in 19. This alone argues for radical surgical removal of the tumor bearing area by gastric resection as soon as the diagnosis is made and the patient is properly prepared. Further confirmation for this policy is afforded by the separate analyses of a small number of benign and malignant cases in which patients were treated either by excision of polyps or by gastrectomy; these show a great superiority of results in gastrectomized subjects.

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DEVELOPMENT OF THE VERTEBRAL COLUMN AS RELATED TO CERTAIN CONGENITAL AND PATHOLOGICAL CHANGES

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A THOROUGH knowledge of the embryology of the vertebral column is essential for understanding diseases of the spine. In addition to obvious malformations, many lesions of later life are based on the complex development of the involved structures. It is the purpose of the present paper to discuss the development of the vertebral column and to point out the embryologic basis of certain confusing lesions encountered in patients. Abnormalities of the neural arch do not fall in the scope of this study.

Most embryologists agree that the notochord is derived from the entoderm forming the chordal plate and very early comes to lie between the medullary canal and the gut (Fig. 1). This notochordal plate is very rapidly surrounded by a condensation of mesenchymal tissue. It finally forms a long, rounded structure extending from the hypophyseal pouch to the tail end of the spine. This chorda is the central structure around which the entire development of the spine occurs. The surrounding mesenchyme forms the perichordal sheath. The mesenchymal tissue also forms the segmented appearing sclerotomes. These consist of a zone of dense caudally situated and a less dense cranially situated zone of mesenchymal cells. The dense zones were called protovertebrae by the early embryologists; a better term is scleromere. Between the dense and the less dense portions a fissure occurs, the fissure von Ebner or intersegmental fissure (Fig. 2). Very early the dense zone (scleromere) forms three processes which extend dorsally, ventrally, and medially. The dorsal extensions form the mesenchymal anlagen of the neural arches, the ventral processes form the ribs or lateral processes and the medial or chordal extensions, toward the notochord, fuse with the perichordal sheath. Later the chordal processes meet around the notochord and form the anlage of the primitive vertebral body. Very early the intersegmental arteries—branches of the primitive aorta—appear between the sclerotomes just caudally to the dense zone of mesenchymal cells. About this time definite membranous structures are formed by the less dense cranially situated portion of the sclerotomes. These membranes are the interdorsal and the interventral membranes connecting the neural processes and the ventral or costal processes. The caudal aspect of the dense, very cellular portion of the sclerotomes then become hollowed out by the cranial portion of the next caudally placed sclerotome. At the same time some mesenchyme enters into this hollowed out area of the dense zone. This interposed mesenchyme together with the previously mentioned less dense mesenchymal zone of the sclerotome forms the anlage of the true vertebral body, while the dense zone now displaced cranially forms the anlage of the annulus fibrosus and the intervertebral disc. The cranial shift is believed to be due to the presence of the intersegmental vessels and the increased nutrition which is available to the cells closest to those arteries. The primitive intervertebral discs now form a membrane which surrounds the anlagen of the vertebral bodies—this membrane is called the interdiscal membrane and it will form at a later stage the anterior, lateral, and posterior longitudinal ligaments of the spine. Coinciding with the formation of the interdiscal membrane the perichordal sheath forms a ventrodorsal extension which divides the true anlage of the vertebral body into two lateral halves.

Most embryologists agree that the true anlage for the vertebral body is formed by the interposed mesenchymes together with a portion of the dense zone of the sclerotome and by

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the less dense cranial half of the next caudal sclerotome. The fissure von Ebner then becomes the true dividing line between the final anlagen of the vertebrae. The intersegmental arteries are situated finally in the midportion of the vertebral bodies.

About the end of the fourth week the anlage of the vertebral body increases rapidly in size and the dense zone now representing the area of the future intervertebral disc becomes thin. The mesenchymal period ends there and the period of chondrification begins. The first centers of chondrification in the body proper occur laterally and are separated by the ventrodorsal extension of the perichordal sheath. This membrane rapidly disappears as the chondrification process progresses.

The notochord, which has been unchanged during the development in the mesenchymal period and which has been present as a solid cord of even size throughout all the mesenchymal and early cartilaginous vertebral bodies and the zones of the annulus, becomes more and more squeezed into the regions of the dense intervertebral discs (Fig. 3). This is due to the increased pressure which prevails during the rapid enlargement of the cartilaginous

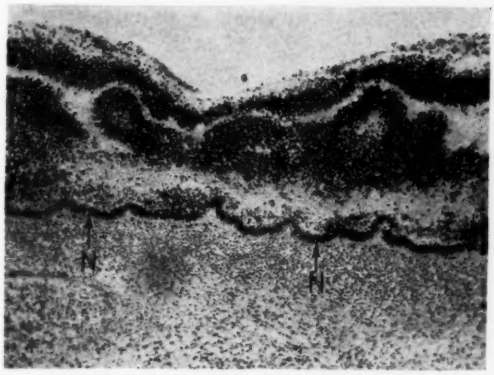

Fig. 1. A human embryo, 3 weeks old, 6 millimeters in length. In the midsagittal section the notochord is well developed, *N*. At this stage the mesenchymal segmented tissue has not surrounded the notochord. The dorsal ectodermal layer, above, is well developed. The notochord has just differentiated from the ventrally situated entodermal tissue, below.

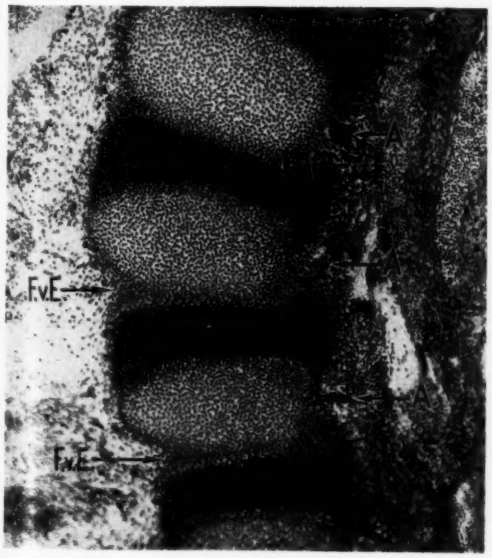

Fig. 2. Four week (1.1 cm.) embryo, Showing dense and less dense portions of sclerotomes with hollowing out of the dense cranial portion by the less dense zone. Fissure von Ebner, *F. v. E.*, well seen dividing the future vertebral bodies. Intersegmental arteries, *A.*, seen situated in midportion of future vertebral body anteriorly.

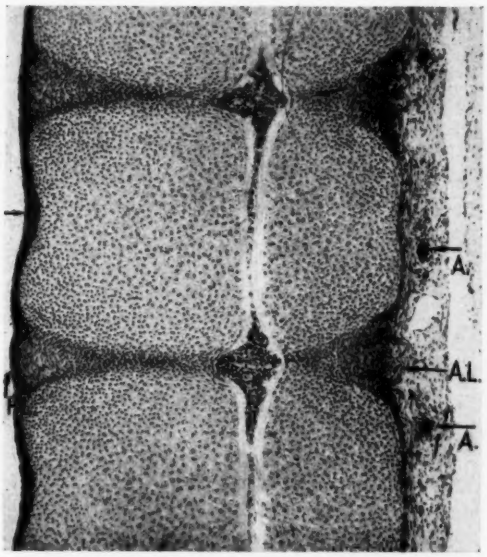

Fig. 3. Nine week (4 cm.) embryo. Displacement of notochordal cells into disc zones, arrow; top. Persistence of mucoid streak. Vertebral vessels seen anteriorly, *A*. Anterior longitudinal ligament, *A. L.*, attaching to vertebral bodies; posterior ligament, *P. L.*, to disc regions. Arrow, left, cartilaginous vertebral body. Note annulus fibrosus anlage.

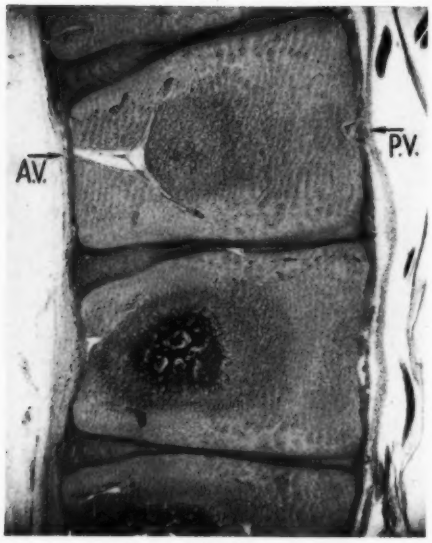

Fig. 4.

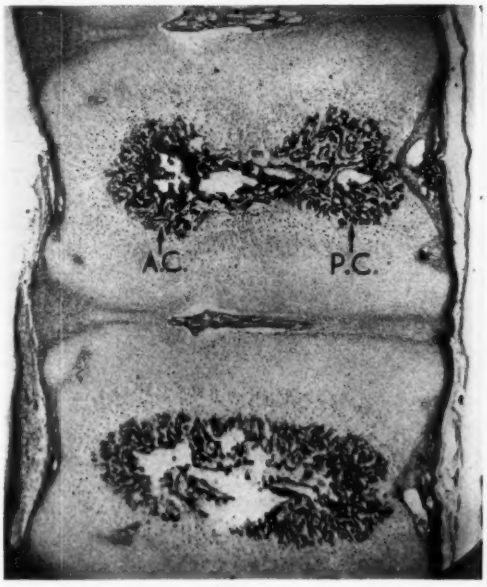

Fig. 5.

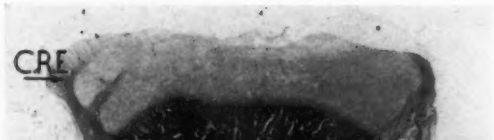

Fig. 6.

Fig. 4. Four lunar month (11 cm. sitting height) embryo, showing ingrowth of ventral, *A. V.*, and dorsal, *P. V.*, vessels into cartilaginous vertebral bodies with early ossification of the cartilage.

Fig. 5. Four month (11 cm. sitting height) embryo. Fusion of the anterior, *A. C.*, and posterior, *P. C.*, ossification centers. Periosteal vessels are seen in the cartilage zones of the vertebral bodies.

Fig. 6. Seven and one-half month (25 cm. sitting height) fetus. Periosteal vessels are seen growing into cartilage plates. Osteoma formation, *O. S. T.*, around the anterior and posterior venous channels. Cartilage remnant, *C. R.*, in one vertebral body. Anterior longitudinal ligament, *A. L.*, is not associated with intervertebral disc tissue but attached to vertebral bodies. Posterior ligament, *P. L.*, *C. R. E.*, cartilaginous ring epiphysis attached to intervertebral disc tissue and not to vertebral bodies.

vertebral bodies. The dense mesenchymal anlage of the annulus fibrosus becomes markedly reduced during the chondrification of the bodies and probably much of the primitive dense annulus actually undergoes chondrification. However, the outermost rim of the disc always remains—dividing the cartilaginous vertebral bodies.

In a 7 to 9 weeks old (1.6-4 cm.) embryo the cartilaginous cells in the center of the vertebral bodies are surrounded by interstitial matrix. At this stage the anterior and posterior longitudinal ligaments are developing and with a connective tissue stain some very

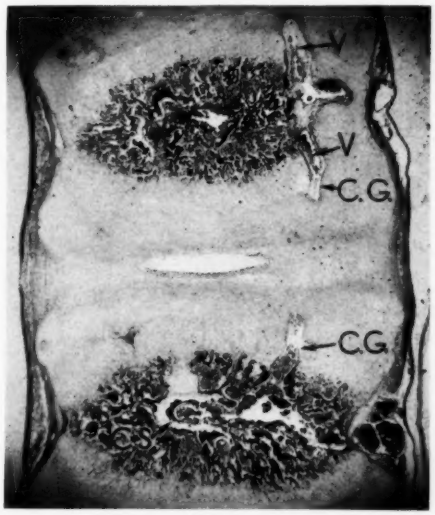

Fig. 7.

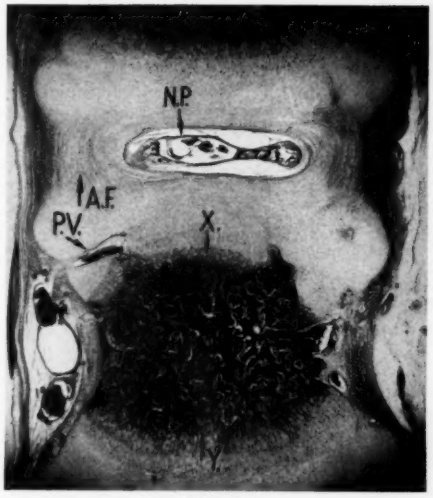

Fig. 8.

Fig. 7. Five and one-half month (19 cm. sitting height) fetus. Vessels, *V.*, coming from vertebral spongiosa perforating cartilage plates. Ring shaped cartilage remnant in one vertebral body, *C. S.*; *C. G.*, chondrification gaps.

Fig. 8. Seven and one-half month (27 cm. sitting height) fetus. Well formed intervertebral disc and vertebral body. Annulus fibrosus, *A. F.*, well developed. Notochordal cells forming nucleus pulposus, *N. P.* Periosteal vessels, *P. V.*, and vessels coming from vertebral body are visible. *x*, Line of endochondral bone formation with chondrification gap; *y*, line of endochondral bone formation.

Fig. 9. Schmorl's node, *S. N.* with rupture of cartilage plate, *C. P.* Protrusion of nuclear material into spongiosa. Reactive bony cup and great amount of proliferating cartilage present.

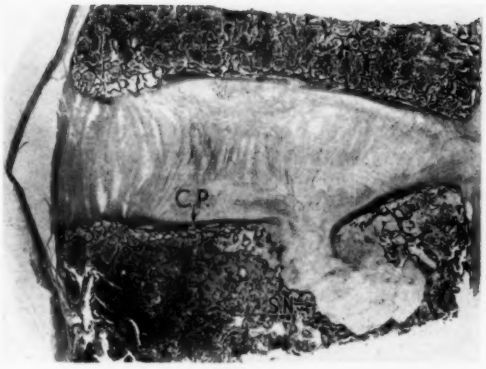

Fig. 9.

early collagen material is visible along the anterior band. The cells in the region of the intervertebral disc arrange themselves in a fashion similar to the ones later seen in the annulus fibrosus. Boehmig (2) states that the local vascular supply has some influence on the direction of growth of these cells. The anterior longitudinal ligament at this stage is more attached to the cartilaginous vertebral bodies while the posterior longitudinal band is firmly attached to the intervertebral disc tissue and is not associated with the posterior surface of the vertebrae. This point was emphasized by Schmorl (21), and it may have some importance in the development of osteophytes in late adult life.

As chondrification of the vertebral body advances, nearly all the notochordal cells are squeezed out from the body proper and are displaced into the disc region where they become enclosed by the dense rim of cells which have not undergone chondrification and which form the true annulus fibrosus. The chordal cells during this period show some mucoid degeneration and some proliferation. The notochordal tissue then forms the early nucleus pulposus.

During this migration of the notochordal cells, the formerly rather thin annulus increases in height. It is noteworthy that in this stage only the notochordal cells are displaced from the developing vertebral bodies.

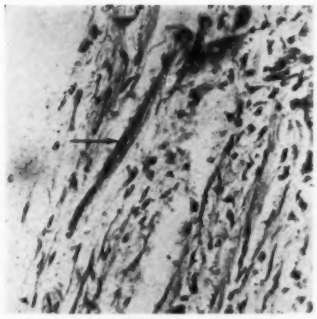

Fig. 10.

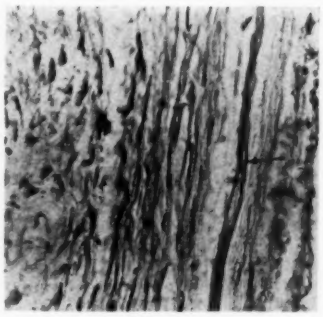

Fig. 11.

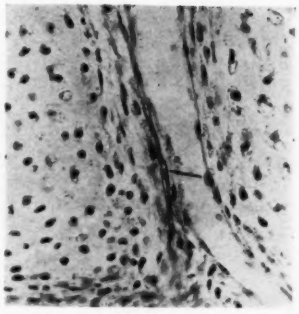

Fig. 12.

Fig. 10. Five and one-half month embryo. Bodian nerve fiber stain. Nerve bundles are seen within the anterior portion of the annulus fibrosus, arrow.

Fig. 11. Five and one-half month fetus. Bodian nerve fiber stain. Arrow indicates site at which nerve fibers are seen beneath the posterior longitudinal ligament.

Fig. 12. Five and one-half month fetus. Bodian nerve fiber stain. Nerve fibers (arrow) are seen within the anterior portion of the annulus fibrosus and the cartilage plates accompanying the periosteal vessels.

The perichordal sheath remains in the center of the cartilaginous vertebrae and forms the mucoid streak. Boehmig (3) has described some variations of the microscopic picture of the notochordal cells displaced into the annulus space as separation of cells into a cranial and caudal part divided by a membrane and also, less often, a dorsal and ventral separation.

In the 9 weeks old embryo (4 cm.) anterior and posterior indentations into the cartilaginous body are produced by periosteal vessels and soon after this stage the cartilage is invaded by these vessels (Fig. 4). Calcification of the cartilage results and is well seen in the 3½ month (9 cm.) embryo preceding the ossification process. The cartilaginous vertebral body is therefore the true foundation for the development of the osseous vertebral body. The invading vessels produce a ventral and dorsal blood lake. In the beginning the ossification centers which are formed dorsally and ventrally in the cerebral body are separated by a cartilaginous septum which persists for a short period of time (Fig. 5). At times this cartilaginous septum will take the shape of a ring (Fig. 7). The ossification proceeds rather rapidly as is well seen in a 4 to 4½ month (11 cm.) embryo. The early centers of ossification which come to lie dorsally and ventrally do not correspond with the centers of chondrification of the cartilaginous stage, the latter being situated early to the left and right of the ventrodorsal extension of the perichordal sheath. The dorsal blood lake and center of ossification enlarges more rapidly displacing the still remaining mucoid streak ventrally. Soon the anterior and posterior centers fuse and form one large center of ossification. The first centers appear in the lower thoracic and upper lumbar region and rapidly extend cranially but less rapidly caudally. The central bone nucleus gives off capillary vessels which are resorbing the cartilage all around it in a star shaped manner. The mucoid streak normally is destroyed by this process, but occasionally remnants will remain. At about the twenty-second to twenty-fourth week of fetal life the ossification center has divided the cartilaginous body completely into two thick cartilaginous plates which show endochondral ossification toward the intervertebral side. At the site of entrance of the vertebral vessels anteriorly and posteriorly, large funnel shaped osseous channels form which, in sagittal sections, appear as bony triangles (Fig. 6). Small osteomas may be formed in those locations. No true cortical bone is seen. Along the anterior and lateral periphery the cartilage plates form horseshoe-shaped structures overhanging the cancellous portion of the vertebral body. It appears wedge shaped on sagittal section and it represents the cartilaginous ring epiphysis. It will form, at a much later stage in young adolescent life, the anlage for the true bony ring epiphysis (rim ledge) or the *Haftepiphyse* of Schmorl. The cartilaginous

Fig. 13.

Fig. 14.

Fig. 15.

Fig. 13. R. van P., Hospital No. 38-25,409, male, age, 29 years, has partial and complete fusion of 10th, 11th, and 12th dorsal vertebrae and fusion of the anterior margins of the bodies of the 8th and 9th dorsal vertebrae.

Fig. 14. Ch. A., Hospital No. B-2464, male, age, 17 years, presents synostosis of 2d and 3d cervical vertebrae posteriorly. Failure of fusion of anterior and posterior ossification centers of 2d and 3d cervical vertebrae. Posterior displacement with wedging of the posterior fused portion. Patient had symptoms of slowly progressing cord compression.

Fig. 15. Th. D., male, age, 8 years. Hospital No. D-3895. Congenital scoliosis. Unilateral wedge vertebra between 6th and 7th dorsal vertebrae.

Fig. 16. Bilateral half vertebrae involving 3d and 4th dorsal vertebrae, in a stillborn, full-term infant. No wedging present.

Fig. 17. L. J., Hospital No. 42-3116, male, age, 22 years. Posterior half vertebra—2d lumbar with wedging.

Fig. 16.

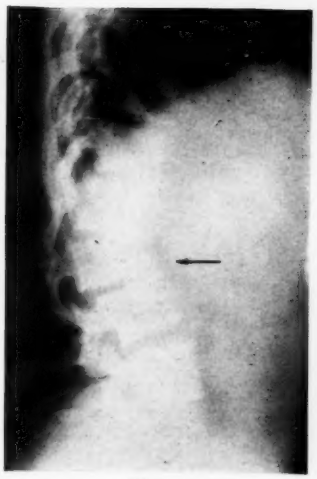

Fig. 17.

ring is the site of insertion of some of the fibers of the anterior and lateral annulus fibrosus, and they will be firmly incorporated as Sharpey's fibers at the time of ossification. No such arrangement is present along the posterior portions of the annulus fibrosus and the posterior margin of the cartilaginous plate.

The understanding of the blood supply and its fate is of special importance for the later understanding of the development of the intervertebral disc. The explanation of some of the nuclear prolapses into the spongiosa of the vertebral bodies occurring at an age when the senescent degenerative changes of the carti-

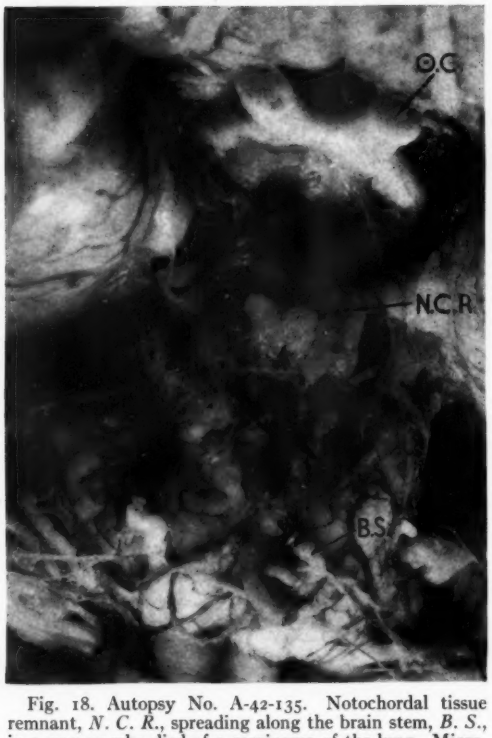

Fig. 18. Autopsy No. A-42-135. Notochordal tissue remnant, *N. C. R.*, spreading along the brain stem, *B. S.*, in a woman who died of a carcinoma of the lung. Microscopically the tissue is identical in appearance with that of a chordoma., *O. C.*, Optic chiasm.

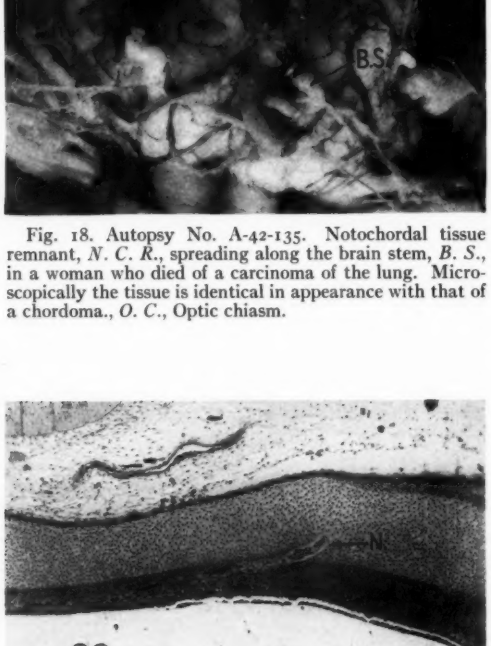

Fig. 19. Seven week (1.6 cm.) embryo. Showing exit of notochord from the basilar cartilage, *N.*, approaching the pharyngeal mucosa. Notochord situated partly outside of the cartilaginous tissue. *O. C.*, Oral cavity, *T.*, tongue, at left, anterior; at right, posterior.

Fig. 20. Seven week (1.6 cm.) embryo. Showing misplaced notochordal cells in tail end of spine (arrow).

laginous plates are only minimal can be based on it. The intervertebral disc is constantly exposed to more or less severe trauma and it is one of the earliest structures to show definite senescent changes. This is partly explainable on the development and the early regression of the vascular supply. In addition to the axial vessels which parallel the notochord, as early as 3½ months (9 cm.), other vessels are derived from the periosteum and penetrate into the cartilaginous plates without entering the central zone of ossification of the vertebral bodies. Uebermuth showed that these vessels enter the intervertebral cartilage at regular intervals all along the rim of the vertebral body and run in the direction of the nucleus pulposus. Those radially placed vessels are responsible for the toothed appearance of the epiphyseal plates of the growing vertebrae and the deep indentation seen in the bony vertebral bodies of the young growing child. Zones of calcification and the numerous foci of ossification develop along these vessels and fuse to form the ring epiphysis. Other vessels coming from the vertebral body penetrate the cartilaginous plates directly, forming anastomotic arcades with those coming from the periosteum (Figs. 7 and 8). A moderate

amount of connective tissue accompanies the vessels into the cartilage. These vascular structures in the cartilage are well seen in embryonic life. Regression and scarring starts shortly after birth and slowly progresses to completeness by the age of 18 to 25 years, at which time most of the growth has stopped and the bony ring epiphysis has fused with the vertebral bodies proper. Where those vessels have penetrated the cartilaginous plates some chondrification gaps result. These are replaced at the time of complete degeneration of the vessels by either cartilaginous plugs or by scar tissue and sometimes by calcification. They form areas of lessened resistance to the increased turgor of the semisolid intervertebral disc substance especially if the disc is subjected to increased pressure. Through these points of reduced resistance nuclear prolapses occur, forming the so called Schorml's nodes (Fig. 9).

Even in the embryo and the very young child at times when the intervertebral disc shows an excellent vascular supply, there is no direct vascular supply to the nucleus pulposus embedded within the annulus. Only the outermost zone of the annulus receives capillary vessels. However, Uebermuth described some brushlike vascular endings which enter this avascular zone. They are supposed to be derived from the previously described vessels.

All of these vessels degenerate gradually, and at 25 years of age none of them remains and the intervertebral disc becomes truly avascular. The only nutrition to the disc following this time is by diffusion processes through the cartilaginous plates coming from the cancellous vertebral bodies. Following this the intervertebral disc is slowly replaced by fibrous and cartilaginous tissue losing its turgor. The maximal turgor and elasticity are present about the 25th and 30th years of life. They decrease more or less rapidly after that time depending on the water content of the disc and annulus. The fate of the nucleus pulposus is also of importance since it forms the noncompressible semifluid medium which is so all important for the proper distribution of the pressure forces over the weight bearing surfaces of the vertebral bodies. Soon after the notochordal cells have all been squeezed into the region of the disc, the cells undergo mucoid degenerative changes and some authors even state that they proliferate. They become clumped together forming a syncytium surrounded by mucoid material. This mass of material is increased soon by the addition of fibrous tissue and hyaline cartilage cells (Fig. 8). Some authors describe fibrocartilage. The notochordal cells can often be demonstrated until adolescent life and older. After the disc becomes completely avascular during the third decade the nucleus pulposus slowly becomes replaced by fibrous tissue and loses the normal semifluid consistency. No vessels enter this structure except those which may penetrate into a severely degenerated disc during repair processes.

The annulus fibrosus, early, shows no evidence of collagen fiber deposition. In a 4 month (11 cm.) old embryo, definite intercellular fibers can be seen all along the periphery of the disc. In a 5½ month (19 cm.) old embryo, the fibers are very well developed and the appearance of the annulus in this stage is that of fibrocartilage. Weigert elastic tissue stains showed no elastic tissue fibers within the annulus during the embryonic life or in an 18 month old child; this differs from the findings of some investigators (4, 13).

Clinically there is evidence (24) that the annulus fibrosus has some nerve supply, but until recent years this has been denied. Jung and Brunschwig (14) demonstrated the presence of nerve fibers histologically beneath the anterior longitudinal ligament (Fig. 10). Recently Roofe showed that some are also present beneath the posterior ligamentous structures (Fig. 11). Sections through a 5½ month embryo stained with the Bodian technique show the presence of large nerve bundles beneath the posterior longitudinal ligament as well as within the annulus fibrosus proper. Nerve fibers beneath the anterior ligament give off fine branches which accompany the periosteal vessels entering the cartilaginous disc substance (Fig. 12). The derivation and the type of these nerves is not clear. Roofe and, earlier, Luschka (nervus sinuvertebralis) state that the posterior bundles are derived from a recurrent branch just distal to the posterior root ganglion. This nerve, after sep-

arating from the main trunk, re-enters the intervertebral foramen and supplies the ligamentous structures two vertebrae lower than the exit of the spinal nerve.

Developmental defects of the spinal column have been poorly understood. One has to differentiate between the malformations occurring in the vertebrae-intervertebral discs column and those along the neural column formed by the neural arches. The latter malformations have a close relationship with developmental defects of the neural tube (6, 7, 8, 9).

Putti at a rather early date attempted to explain many of the defects on the basis of the mesenchymal and cartilaginous state of embryonic development. However, many of his conclusions were based on animal observations which do not correspond with the embryology in the human. Junghanns (15, 16) has given a very excellent summary which contains some very good schematic drawings and explanations. Not all the developmental defects in the vertebrae-disc column can be explained on the basis of malformations in the mesenchymal and cartilaginous embryonic states. Many, however, become very easily understandable if one considers the vascular supply and the changes which occur in the notochord during the different stages.

Congenital synostosis (*block vertebrae*). There is complete or partial congenital bony fusion of two or more vertebral bodies without evidence of any or only small amounts of interposed intervertebral disc tissue (Figs. 13 and 14). This may be on the basis of complete chondrification of the dense mesenchymal zone which would normally form the annulus fibrosus. The cartilage bodies of the preosseous vertebrae fuse, and they become ossified in one mass after the periosteal vessels penetrate into the cartilage. This malformation is then on the basis of a complete regression of the primitive annulus fibrosus.

Sagittal cleft vertebrae. Persistence of the ventrodorsal extension (10, 11, 23) of the perichordal sheath with or without the persistence of the chorda or splitting of the notochord (6, 7, 8, 9) in this area may prevent fusion of the laterally situated cartilaginous vertebral halves. Each half may become ossified separately by its anterior and posterior centers with persistence of the sagittal cleft. With weight bearing in later life, such vertebrae may form the "butterfly vertebral bodies."

Lateral half vertebrae or wedge vertebrae. At times only single lateral half vertebrae are seen (Fig. 15). Feller and Sternberg (6, 7, 8, 9) believe that they have their origin in the cartilaginous state of the embryonic life and they have observed that the chorda shows a curvature toward the side of the half vertebrae with absence of cartilaginous development on the other. Junghanns and others (17) believe that the origin of the half vertebrae is on the basis of lack of blood supply to the missing half of the body. At first those half vertebrae are cuboidal in shape, but they become a wedge as soon as weight bearing occurs. Bilaterally occurring half vertebrae may involve large segments of the spinal column as wedged hemivertebrae at different levels (Fig. 16). They are placed one on each side and will give in later life a bilateral bony scoliotic curve. They are most commonly explained on the faulty unilateral cranial hemimetameric shift of the vertebral segments which occurs in the blastemic period. This unilateral occurring shift will cause an anlage for a half vertebra to remain at the lower and the upper end of the unequally shifted column which will later undergo chondrification and ossification.

Ventral and dorsal half vertebrae. These are rare (Fig. 17). The explanation for these must be on the basis of faulty vascularization and agenesis of either the anterior or posterior center of ossification. They fuse normally early. The rôle of the notochord in these cases is not quite clear. Feller and Sternberg believe that the notochord is missing in these places. It is logical to assume that the lack of vascularization of either the anterior or the posterior portion will cause either one of them to remain in a cartilaginous state. The malformed vertebral bodies will at times take the form of wedges as soon as weight bearing is started. The deformity resulting will be of the gibbous type.

Malformations of the chorda and chordal remnants. During the state of migration of the notochordal cells during the cartilaginous period of embryonic development, there is definite persistence of the perichordal sheath form-

ing the mucoid streak. Anywhere along the course of this structure which normally regresses completely during the ossification of the vertebral bodies, chordal cell remnants may be found (Fig. 3). These remnants have been found and reported nearly everywhere in the spinal column. One of the more frequent abnormalities seen are the outpouchings of the otherwise normal intervertebral discs which is usually associated with thinning of the cartilage plate in the zones where the mucoid streak entered the intervertebral disc. Those weakened places are often the site of centrally placed nuclear prolapses into the adjoining vertebral bodies. Sometimes true extensions of the nuclear material in a wedge-like manner can be seen protruding into the vertebra. A few cases have been reported in which the complete chorda has persisted as a solid central mass connecting two or more intervertebral discs.

During postmortem examinations notochordal tissue remnants are present in 2 per cent of the cases. Most of these are found in the region of the clivus at the base of the skull (Fig. 18). The notochordal cells during the normal development are doomed to undergo degeneration if they remain enclosed within cartilaginous or fibrocartilaginous tissue. This is obviously the case in the normal intervertebral disc and no notochordal cells are seen after the late adolescent period. In certain areas as in the notochordal extension within the base of the skull and in the sacrococcygeal region only a moderate amount of cartilaginous tissue will surround the chorda. In a few places the notochord normally is situated outside of dense mesenchymal or cartilaginous regions during the embryologic development. This is the case at the roof of the oral cavity where the chorda enters into close relationship with the lining pharyngeal mucosa (Fig. 19). It also comes to lie rather free just posterior to the hypophyseal pouch. Another area is close to the foramen magnum and the odontoid process. The same is true in the region of the rather undifferentiated tail end of the spinal column where only very rudimentary vertebrae are formed by the mesenchymal tissue and the cartilaginous and ossification processes (Fig. 20). In these areas some blood supply may be retained and the notochordal cells fail to degenerate. These are the locations where in adult life most chordomas occur. Occasionally they have been reported along the spinal column. The latter can be explained on the basis of remnants included in the vertebral bodies where the blood supply is maintained.

Congenital weaknesses of the cartilage plates. In areas where the cartilage plates are penetrated by vessels from the vertebrae, mostly along the peripheral two-thirds and in the center where the axial vessels accompany the notochord, chondrification gaps develop (Figs. 7 and 8). These are evident in the embryonic sections and in sections through the adolescent intervertebral discs. These areas form points of lessened resistance to the increased turgor of the nuclear material and at times, the latter will be forced through these gaps to form spongiosal prolapses (Fig. 9). If this occurs during the actively growing state of the adolescent period the process will be a rather gradual one stimulating considerable cartilage formation, but little reactive bone. Thus, often no reactive bony cup can be seen early in the x-ray pictures. Also, no true tears of the cartilage plate will result. In older persons after the growth period has ended, the prolapsing material is more of a fibrous nature and the reparative process proceeds rapidly to reactive bone and a bony cup becomes visible in x-ray pictures.

Multiple spongiosal nuclear prolapses with juvenile kyphosis in the young adolescent groups occur mostly in boys subjected to very heavy manual labor. One must keep in mind that at this age there is still good blood supply to the intervertebral disc tissue and not all the vessels have degenerated. The nucleus pulposus is still rather liquid and easily displaced. Scheuermann, basing his observations and this theory only on x-ray findings, states that the deformity is due to an aseptic necrosis—an "epiphysitis" of the ring epiphysis which is undergoing marked ossification at about this age. Schmorl and since then others (22) have examined, at autopsies, numerous spines of adolescent patients with juvenile kyphosis, and they found large nuclear prolapses into the spongiosa through the cartilage plates. These prolapses are in a location which is

usually the one where some of the chondrification gaps have occurred due to degenerated vessels producing weak points. It also has been proved fairly conclusively that the ring epiphysis has nothing to do with the growth in the height of the vertebral bodies. This growth in the height is exclusively a function of the cartilage plate which is central to the ring epiphysis and underlies the rim ledge proper. Nuclear prolapses of juvenile kyphosis often occur all along the vertebral bodies of the lower thoracic and upper lumbar region. The uneven growth in height of individual vertebrae tends to retard the growth anteriorly where the increased pressure load is concentrated. More normal growth occurs posteriorly. Thus, the relative wedging of the vertebral bodies is secondary to the improper mechanical function of the degenerating narrowed intervertebral disc. In this way the kyphotic deformity results. The fragmentation of the anterior portion of the ring epiphysis seen in x-ray pictures results from improper motion, abnormal pressure relationship, and shearing stress put upon the anterior annulus fibers and the unfused ring epiphysis.

SUMMARY

An attempt has been made to describe and illustrate the development of the vertebrae and the intervertebral discs, and to correlate developmental peculiarities with certain lesions found in later life.

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MESONEPHROMA OR TERATOID ADENOCYSTOMA OF THE OVARY

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THE etiological relationship between the various residual elements of the wolffian body which survive in the adult and gynecological neoplasms has always been an interesting one. The origin of certain cysts and tumors from the remnants of the wolffian duct system has been generally accepted but until Schiller (16) in 1939 described a semisolid ovarian tumor of the ovary and postulated the mesonephros as providing the background for its development, the wolffian body itself has not been seriously considered as a source of ovarian neoplasms. There seems to be no theoretical reason why mesonephric tumors should not develop in the ovary or the tissue adjacent to it particularly as tumors of adrenal cortical cells of the ovary and mesovarium are well recognized. In fact, it would seem more difficult to explain why tumors of the wolffian tubular system are not the source of neoplastic phenomena in the ovary. Such tumors in retroperitoneal regions are well known and their morphological characteristics as well as their mode of growth and life histories have been described in considerable detail. The question raised by Schiller is therefore one of great interest, and additional information is needed in order to prove or disprove the thesis which he has proposed.

Although 3 years have elapsed since the original contribution only a few papers have appeared upon the subject, notably those of Jones and Seegar (7, 8); Kazancigil, Laquer and Ladewig (11); Tuta and Siebel; and that of Rosenblatt and Grayzel. In all, 30 instances of so called "mesonephroma ovarii" have been studied and reported which appear, at least in part, to fulfill the criteria outlined by Schiller. We wish to report 10 more ovarian tumors which seem to us to fall into this category.

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A study of the previous reports upon this subject indicates that although nearly all writers agree that a characteristic tumor of the ovary has been described having a characteristic morphology in many respects, which for the time being should justify its being placed in a special category, there are reservations as to its etiological relationship to the mesonephros. Jones and Seegar state that "the theory of the mesonephric origin of these tumors, while plausible is not yet proven." Their skepticism is based largely upon the absence of "glomerular" bodies in the tumors studied by them. They come to this conclusion although the general structure of the tumors was in other respects remarkably similar to those of Schiller's report. Kazancigil and coworkers report a study in which they made serial sections through glomerulus-like structures, without finding anything that resembled a vascular tuft. Such an observation, although not necessarily conclusive, is to us significant. On the other hand, the failure to demonstrate a structure so highly differentiated as a glomerular capillary bed in a neoplasm cannot be considered as final proof that there is no relationship to the mesonephric organ.

In our series of tumors we have usually been at a loss to demonstrate structures which even remotely resembled the architectural arrangement of wolffian glomeruli. It is true that the tumors abounded in acini into which papillary tufts of epithelium projected with or without a supporting connective tissue stalk; but one would be as justified in naming any one of several well recognized ovarian or uterine tumors as "mesonephric" if the demonstration of this arrangement of cells were to be taken as the criteria of such origin.

Retroperitoneal wolffian tumors on the contrary, such as have been described by many writers, are characterized by much more definite glomerulus-like structures. The literature

goes back to 1894 when Frank reported his studies. Hinman, Gibson and Kutzmann in 1924 and more recently Hardeman and De Groat have all emphasized the point that "one definite criterion of mesonephric origin is the presence of the primitive glomeruli or renal tubules."

Although most of the ovarian tumors reported have been characterized by closely packed acini lined by low cuboidal epithelium which could easily be interpreted as a formation of wolffian tubules, the infrequency or dearth of the "glomerular" structures is significant. It is difficult to believe that the ovary offers an environment so different from the retroperitoneum as to produce a relative lack in glomerlus formation while allowing at the same time a profuse growth of ducts.

We are skeptical, therefore, of Schiller's explanation of the etiology of this group of tumors and prefer not to accept his term, mesonephroma ovarii, for them. We are, on the other hand, convinced that they are not rare, that they form a morphologically distinct group of ovarian tumors with a characteristic life history and that they should, for this reason, have a distinctive name and more important that they should be studied as such so that more can be learned about them.

We are at variance with those who have expressed the belief that these tumors are merely a hydropic form of serous cystadenoma, for these tumors almost invariably produce a mucin-like substance which reacts to the usual stains for mucin. While the mucin stain is nonspecific, the fact that it is positive in these tumors serves to differentiate it from the serous group in which it is not positive. At the same time this finding indicates a probable relationship to wolffian or teratoid antecedents. On the other hand, these neoplasms are quite different morphologically from the pseudomucinous cystadenomas, as well as different in their mode of growth. Whether benign or malignant, they are essentially solid tumors which tend to become cystic only as they degenerate.

CASE REPORTS

Case 1. Miss A. S., No. 182234, 50 years of age, single, was admitted to the New York Hospital on October 4, 1937, complaining of suprapubic pain and dull ache; pain on the inner aspect of the right thigh; and a feeling of something rubbing on the inside of the abdomen. These symptoms had been present for 6 months. She had had no postmenopausal bleeding since uncomplicated menopause 7 years previously. Examination revealed a movable and nontender abdominal mass arising from the left pelvis and extending up to two fingerbreadths below the umbilicus. On October 6, 1937, a subtotal hysterectomy, a right salpingo-oophorectomy and a left salpingo-oophorocystectomy were performed. The large cystic left ovary, right ovary, broad ligament, and omentum were involved in tumor tissue. The patient received postoperative radiation before discharge from the hospital. Within 2 months, the patient was in a hopeless state with extensive recurrence of the tumor.

Pathology. The tumor tissue consisted grossly of papillary and cystic structures with infiltrating hemorrhage. The left ovarian cyst measured 13 by 11 by 8 centimeters, the lower pole of which was papillary and semisolid. Microscopically, the tumor tissue was lobulated, encapsulated, and supported on a fibrous connective tissue framework. In some areas in solid sheets, elsewhere semicystic and necrotic, the tendency toward a fairly typical and high cellular acinar arrangement prevailed. Fibrous papillary processes containing nests of the typical acini were also seen; the acini, as in the other tumors listed below, contained mucin-like material. The individual cells were of a fairly uniform pattern, not markedly basophilic, and were arranged in a single, though oftimes crowded, row. Nuclei were open, pyknotic and clearly delineated. Occasional mitoses were seen. In one section (Fig. 3) there were resemblances to papillary serous cystadenoma.

Case 2. Mrs. R. W., No. 102297, 43 years of age, primipara, white, with a normal menstrual history, complained, on admission to the New York Hospital on November 7, 1937, of an enlarging "lump" in her abdomen which had been present for 6 months. There was associated fatigue and a 10 pound weight loss. Examination revealed a mass arising in the pelvis and extending to the umbilicus. It was movable, nontender and nodular. At operation, 2 days later, the large ovarian tumor together with both tubes, right ovary, and fundus of the uterus were removed. There was no evidence of metastasis. She received postoperative irradiation. She is to date in good health and has no evidence of recurrence.

Pathology. The uterus, right tube and ovary appeared normal. The left tube stretched over an encapsulated ovarian tumor measuring 12 by 12 by 16 centimeters. On section, the semisolid tumor in its central portion was of gelatinous character. Elsewhere it was made up of solid whorls of yellowish tissue. Microscopically, within a fibrous capsule on a fibrohyaline stromal background were nests, clusters, and sheets of epithelial elements. Although the characteristic alveolar structures of Schiller tumors were readily found, there was a tendency toward

luteinization so much so as in some areas to simulate granulosa cell tumor of the Lecène type (Fig. 4).

CASE 3. Miss M. A., No. 245875, 19 years of age, Italian, was first admitted to the New York Hospital on September 21, 1939, with an enlarging abdominal tumor of 4 months' duration, suspected by the patient as being due to pregnancy. Examination disclosed a firm, cystic, and smooth mobile tumor filling the cul-de-sac and extending into the abdomen. At operation 5 days later considerable free fluid was found in the abdomen; the left ovarian cyst and tube were removed. She remained free of symptoms until one week prior to her second admission (May 12, 1940) at which time there developed pain and swelling of the abdomen. A right adnexal semicystic mass was noted to extend from the cul-de-sac to the umbilicus. The following morning, a laparotomy was performed. Extensive tumor involvement was noted, only part of which could be removed. The patient did poorly thereafter and died on July 19, 1940. Autopsy permission was not granted.

Pathology. The original specimen consisted of a collapsed thin walled and multilocular cyst measuring 10 by 16 by 12 centimeters. The internal surface had many elevated solid areas, some of which were infiltrated with hemorrhage. Gross material from the second operation was very soft, loosely organized, and friable. Mucin-like material exuded from the cut surface. Microscopically, the appearance was of a loose and irregular arrangement of the delicate epithelial cells, with some tendency toward acinar and gland-like formations. Mitoses were not infrequent. There was little stromal tissue and this was of varying density. Considerable necrosis and degeneration were noted in some areas.

CASE 4. Mrs. M. S., No. 24048, 64 years of age, was admitted to the New York Hospital on June 20, 1940, because of swelling of the abdomen, ascites, and abdominopelvic tumor. Eleven months previously a lower abdominal tumor was incidentally found during a hernioplasty. Follow-up at that time was refused by the patient. On June 26, at operation, a large adherent left pelvic tumor together with the left tube and ovary was removed. Liver metastasis were noted at that time. Following discharge, her course was slowly downhill. She was readmitted on November 11, 1940, and died 5 days later. Autopsy revealed widespread tumor involvement of peritoneal cavity and metastases including involvement of liver, bowel, spleen, and pleura.

Pathology. The operative specimen was a multilocular semisolid ovarian cyst with penetrating tumor tissue, measuring 16 by 13 by 10 centimeters. On section, papillary neoplastic tissues were found in several loculi. Throughout the microscopic pattern was quite characteristic. The typical epithelium lined cysts and acini varied greatly in size. Some contained considerable epithelial elements and appeared superficially as glomeruli. Careful examination did not bear this out. A fibrous background was present and in a few areas there was some evidence of tendency toward papillary serous cystadenoma.

CASE 5. Miss H. S., No. 291061, 68 years of age, was known to have an abdominal tumor for 2½ years, prior to her first admission to the New York Hospital on March 25, 1941. More recently she had complained of pain in the lower abdomen and groin, and of a 25 pound weight loss. Examination revealed ascites and a large cystic mass filling the lower abdomen and pelvis. At operation 2 days later the large left ovarian tumor together with the right ovary, both tubes and fundus of the uterus was removed. Pelvic implants were noted. Postoperative x-ray therapy was given. Recurrence was evident 7 months later; and in November she was readmitted in a cachectic state. At that time a right lower quadrant abdominal tumor was palpable. The patient was discharged temporarily improved after a 2 weeks' hospital stay.

Pathology. The tumor measured 12 by 17 by 20 centimeters. At one pole the capsule was penetrated by a friable, solid mass. On section, a large cyst filled with thick dark brown material was noted; elsewhere the tumor was solid. Microscopically, the tissue was highly cellular with sheets of delicate epithelial cells. In some areas there was an attempt at acinar formation. Elsewhere it was less differentiated and in these, where cells were closely packed, the cytoplasm appeared clear due to hydropic degeneration. The adenomatous areas were typical (Fig. 2), and served to classify this tumor with the "mesonephric" group.

CASE 6. Miss J. B., No. 25123, 52 years of age, a nurse, was admitted to the New York Hospital on April 9, 1941, because of symptoms of intermittent groin pains of 5 months' duration, and with the finding of a moderately tender, firm, round mass the size of an orange in the left pelvis. At operation 5 days later a left broad ligament cyst together with the left ovary, fundus of the uterus, and appendix, was removed. Postoperative radiation was given. When last seen 7 months later, the patient was in good health and there was no evidence of recurrence.

Pathology. The collapsed cyst must have measured 7 centimeters in diameter. It was lined with cake-like projecting masses which on section were found composed of yellowish material. No tumor tissue was found in the other specimens. Microscopically, the tissue consisted largely and quite uniformly of typical cells. They were arranged in nests and acini separated by thin fibrous septa. The whole tumor was well differentiated.

CASE 7. Mrs. B. S., No. 6557, 51 years of age. Because of a known myomatous uterus this patient had been followed carefully since 1933. A large abdominopelvic tumor extending to the umbilicus was first found at her regular 6 months visit in April 1941. She complained, on admission to the New York Hospital, of pressure symptoms of 1 month's duration. At operation on May 6, 1941, the large left cystic ovarian mass and myomatous uterus, together with both tubes and right ovary were removed. Her postoperative course was uneventful and she is to date free of evidence of recurrence.

Pathology. The semisolid ovarian cyst measured 8 by 9 by 10 centimeters. No penetrating growth was evident. On section, the multilocular cyst contained gelatinous material; its center was solid. The uterus contained several myomas. The other specimens were not remarkable. Microscopically, there was an extensive fibrous and hyaline supporting tissue. Scattered through this were segregated nests of epithelial structures, some of which had an alveolar pattern. Papillomatous areas were also present which, like those of Case 4, simulated serous cystadenoma. However, material in acini and interpapillary spaces was found which responded to mucin stains.

CASE 8. Mrs. E. A., No. 60096, 30 years of age, on admission to the New York Hospital on July 5, 1942, gave a history of a noticeable enlargement of the abdomen associated with some recent right lower quadrant abdominal pain for the last 6 months. Examination revealed a large cystic mass arising in the pelvis and extending to the xiphoid. Two days later at operation, the large cystic right ovary together with both tubes, left ovary, and uterus was removed. No extension or implants were found. She received postoperative radiation and was discharged apparently well.

Pathology. On gross examination, the cyst was found to be unilocular, about 20 centimeters in diameter. The wall contained several papillary areas, many degenerative. Microscopic sections of several areas showed the typical pattern with clusters, papillary and acinar groupings of epithelium-like cells. The larger clefts and spaces contained débris and a precipitated mucinous material. Considerable degeneration was also present.

CASE 9.[1] Mrs. M. W., 48 years of age, complained of pain in the right lower quadrant of the abdomen for 2 months. A tender mass of 10 centimeters in diameter was found. At operation on November 17, 1941, a subtotal hysterectomy, right salpingo-oophorectomy, left salpingo-oophorocystectomy and appendectomy were performed.

Pathology. The thin walled multilocular ovarian cyst weighed 258 grams and contained clear and mucinous material. Into the larger cyst an irregular mass 10 by 3 centimeters projected. The other specimens were not remarkable. Microscopically, sheets and clusters of epithelial cells, in some areas with clear cytoplasm like those in luteinized granulosa cell tumors, were found. There were scattered divisional fibrous septa. Elsewhere areas were present in the sections which were clearly recognized as thecoma. However, in other parts, a characteristic arrangement of the cells typical of the so called "mesonephric" tumor was seen and served to classify this with the group. Considerable necrosis was spread throughout the several fields.

CASE 10.[2] Baby S., 11 months old, because of vaginal bleeding for 5 months, was examined by a gynecologist and biopsy specimen of a vaginal fornix tumor was taken. Extensive radiation was given; notwithstanding, vaginal bleeding recurred 7 months later and examination disclosed recurrence. Radiation was repeated but without effect. The infant died at age 22 months, December 20, 1938. Autopsy revealed extensive pelvic mass; metastases to liver, lungs and mediastinum.

Pathology. Under low power magnification, there was less resemblance to the classical picture in these scattered small nests and acini of epithelial cells in a fibrous background. However, on careful scrutiny under high power, the epithelial cells were typical and found to line the acini in the characteristic crowded single and multilayered fashion. Necrosis and degeneration was extensive.

[1]Reported through the courtesy of Dr. George Shank, of Toronto.
[2]Reported through the courtesy of Dr. Nicolas Alter, of Jersey City.

GENERAL DESCRIPTION OF THE TUMORS

The tumors occurred in the left ovary in all but 2 instances. The ages of the patients ranged from 11 months to 68 years; one was an infant, another was 19 years, and all the rest were over 30 with the oldest 68 years.

Usually the growth is oval in shape measuring from 3 to 17 centimeters in the smallest diameter. The capsule is ordinarily varied in thickness being thin and bosselated over the cystic areas and more dense over the solid portions. Occasionally, papillary processes penetrate the capsule and appear on the external surface. However, generally the external surface is smooth and free of growths or adhesions.

The inner aspect of the tumors present multiple cysts of different sizes and a solid portion which is usually situated on one side of the cyst. In the solid portions are areas of recent growth which are pinkish-gray in color; elsewhere they are largely composed of rather soft grayish-yellow tissue and often contain areas of degeneration. Fatty degeneration, as proved microscopically by fat stains, is in

Fig. 1. Camera lucida drawing (high power magnification), showing the characteristic adult acinar structure of teratoid adenocystoma. Note the typical hydropic epithelial lining cells, arranged in single and multilayered manner.

Fig. 2. Photomicrograph of a well differentiated tumor showing alveoli with single layered epithelial lining. Several intra-alveolar spaces contain a mucoid material. (Hematoxylin and eosin stain. × 20.)

Fig. 3. Photomicrograph of a papillomatous area with stalks and papillae covered by typical epithelium. (Hematoxylin and eosin stain. × 20.)

Fig. 4. Photomicrograph of an undifferentiated tumor. Immature cells are closely packed in sheets, separated by thin fibrous septa. Note the light staining cytoplasm of the older cells. (Hematoxylin and eosin stain. × 20.)

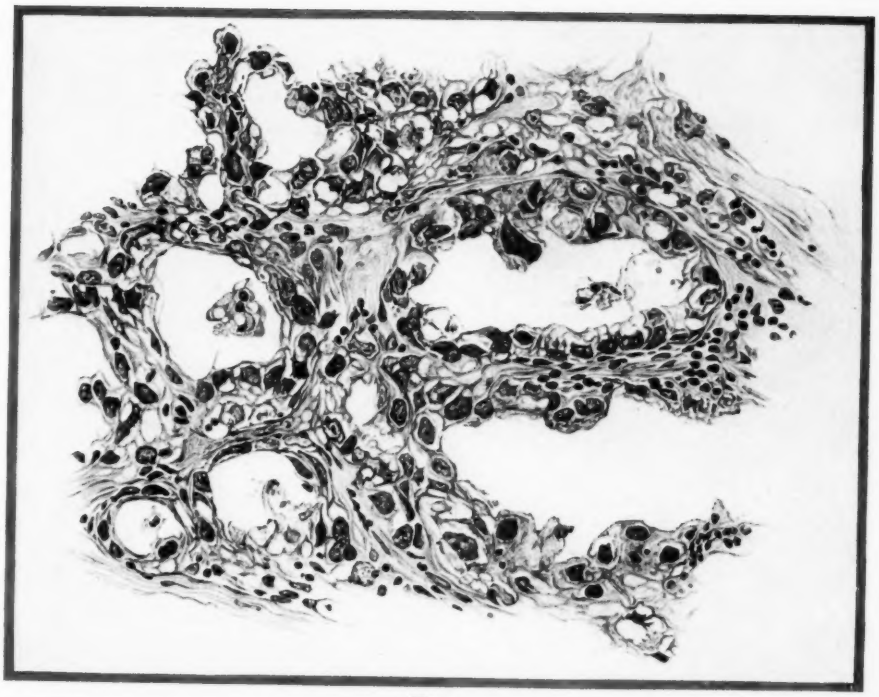

Fig. 1

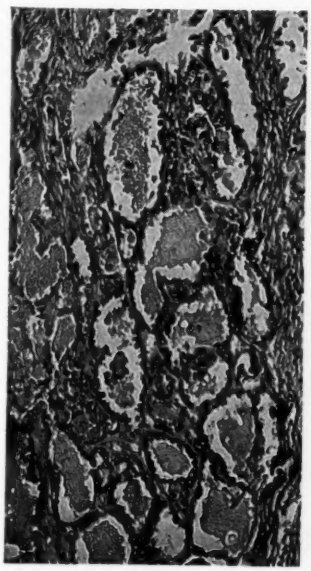

Fig. 2

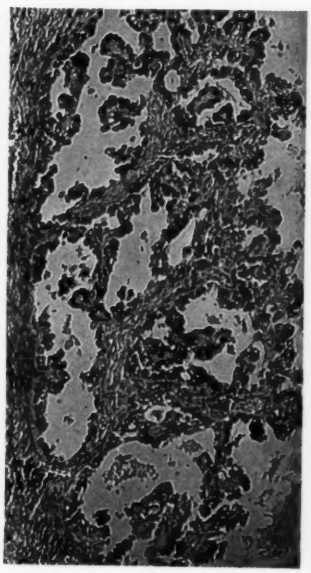

Fig. 3

Fig. 4

Mesonephroma or Teratoid Adenocystoma of the Ovary.—William B. Stromme and Herbert F. Traut

TABLE I.—SUMMARY OF TEN CASES REPORTED

Case number	History number	Age	Symptoms	Clinical findings	Operative findings	Primary site	Treatment	Result
1.	182234	50	Suprapubic pain; pain inner aspect right thigh, 6 mos.	Abdominopelvic mass rising to two fingers below the umbilicus	Adherent papillary and semisolid cyst with penetration and metastases	Left	Operation	Recurrence 3 mos.
2.	102297	43	Mass in the abdomen 6 mos. Weight loss and fatigue	Abdominopelvic mass extending to the umbilicus	Encapsulated tumor 12x 12x16 cm. Semi-solid	Left	Operation and x-ray	No recurrence, 4 yrs.
3.	245875	19	Enlarging of abdomen; left lower quadrant pain; 4 mos.	Cystic tumor from cul-de-sac to the umbilicus; ascites	Ruptured cyst 10x10x12 cm.; thin walled, multilocular and hemorrhagic	Left	Operation	Died in 10 mos.
4.	24048	64	Swelling of abdomen, 3 wks. Swelling of left groin, legs; anorexia	Large firm abdominopelvic tumor. Ascites	Semisolid cyst 16x13x10 cm. with papillary penetration; ascites. Autopsy: Widespread involvement with distant metastases	Left	Operation	Died in 5 mos.
5.	291061	68	(1) Abdominal tumor 2½ yrs. Pain groin and abdomen 3 mos. Weight loss. (2) Nausea, vomiting, constipation	(1) Cystic mass filling lower abdomen and pelvis. (2) Recurrent tumor on right. Bowel obstruction	Semisolid tumor 12x17x 20 cm. Penetrating friable tissue. Pelvic implants	Left	Operation and x-ray	Recurrence in 7 mos.
6.	25123	52	Intermittent groin pains of 5 mos.	Firm round mass left lower quadrant, size of orange	Smooth walled cyst 7 cm. in diameter	Left	Operation and x-ray	No recurrence 7 mos.
7.	6557	51	Urinary frequency, incontinence, nocturia; dull lower abdominal ache, 1 mo.	Firm irregular fixed tumor from vaginal fornix to umbilicus	Multilocular semisolid cyst 8x9x10 cm. No penetrating growth	Right	Operation	No recurrence 5 mos.
8.	60096	30	Enlargement of abdomen and right lower quadrant pain 6 mos.	Large cystic mass filling pelvis and abdomen	Single cystic mass 20 cm. in diameter	Right	Operation and x-ray	Discharged well after 5 wks.
9.	Gift	48	Pain, right lower quadrant, 2 mos.	Tender mass of 10 cm. diameter	Double cyst with no penetration	Left	Operation	?
10.	Gift	11 mos.	Vaginal bleeding, 5 mos.	Vaginal fornix tumor	Autopsy revealed extensive pelvis masses with distant metastases	?	X-ray	Died in 11 mos.

evidence with free fat in the intercellular and intra-alveolar spaces. Intracellular fat droplets are also seen in such locations. The cysts and cut surface of the solid portion of the tumor yield a shiny mucoid material, which is precipitated by both alcohol and acetic acid and stains in the tissues with thionin and mucicarmine.

The tumors probably are slow in rate of growth as our patients gave histories indicating the presence of the tumors from 6 months to 4 years.

Extension of the growth may be by implantation of papillary processes upon adjacent peritoneal structures followed by dissemination throughout the abdomen or the metastasis may be by way of the lymphatics. Free abdominal fluid is not a constant finding even when peritoneal involvement is present; however, it may occur. The omentum may be the only abdominal structure containing gross metastases. However, extensive bowel implantation as well as nodules in the liver, spleen, and pleura were found.

MICROSCOPIC STRUCTURE

The larger cysts are usually lined by a single row of flattened cuboidal cells, while the smaller ones have a hydropic appearing epithelium in a single row, the cells being of varying heights depending upon their secretory activity.

The solid or semisolid tissues exhibit varying degrees of differentiation; the more adult types (Figs. 1, 2) consisting of closely packed acini resembling tubules (collecting ducts?) lined by a single row of hydropic epithelium. Occasionally the acini contain papillary structures extending into them, consisting of one or more layers of columnar cells resting upon a

delicate connective tissue stalk. In the papillary tumors one can often demonstrate portions of the tumor in which large connective tissue structures are found lined by a single row of flattened epithelium resembling the serous type of growth seen in serous cystadenomas (Fig. 3). Doubtless it is this morphological variation which has led to the feeling in some quarters, that the so called "mesonephroma ovarii" is a type of serous tumor. With this view we cannot agree.

In less well differentiated tumors (Fig. 4) papillarity increases and the formation of acini decreases until in the least differentiated specimens, the cells may lie in solid sheets.

The character of the epithelium is varied, depending upon age, secretory activity, and degree of differentiation. The older epithelial cells may be quite low and having little cytoplasm may present a marked basophilic reaction. The young actively secretory cells, on the other hand, often are filled with fluid and have a very hydropic appearance. In this stage the product of secretion takes the usual mucin stains. When secretory cells are packed in close sheet formation the hydropic cytoplasm gives them an appearance resembling lutein or adrenal cortex cells. However, they do not stain with Sudan III.

Our efforts to demonstrate glomerulus formation were not rewarded by the finding of convincing structures. Perhaps we expected too much in searching for something which looked like a simplified wolffian glomerulus. However, we have been guided by the illustrations of wolffian tumors as reported by many writers, including Hinman, Gibson, and Kutzmann.

The more malignant tumors as judged by the clinical course of the patient were those showing some papillary development and particularly those which were highly cellular and more completely undifferentiated.

It should be pointed out that from a morphological point of view, these tumors can assume a variety of histological pictures and for this reason there will be those who will conclude that all of the tumors reported cannot have a common etiology. However, a study of tissues taken from all portions of the tumors leads us to believe that the major portion of them represents a common type of epithelial cell and that in general their variation in arrangement is such as might be expected as being due solely to variations in neoplastic differentiation.

One tumor, however, contained areas of undoubted theca and granulosa cells and another had areas which morphologically resembled the serous cystadenoma. Inasmuch as we believe that the so called "mesonephromas" are in all probability teratoid cystadenomas, the finding of cells of various types is not only to be expected on occasion but we should anticipate that as other studies of these tumors are reported they will become a much less clearly defined group of tumors. In our opinion, it is only the well differentiated type of tumor which closely simulates the morphology as outlined by Schiller.

CLINICAL COURSE

Six of the 10 patients are dead or have extensive recurrence of the growth, indicating a high degree of malignancy. The other 4 patients have no recurrence thus far although it is too early to assume a sanguine attitude toward their future.

All of the patients received surgical treatment and 6 of these were given extensive postoperative x-ray radiation. Neither surgery nor the x-ray seems to have had any effect in prolonging the lives of the patients having the less differentiated type of tumor. A table is provided giving the main clinical and pathological characteristics.

SUMMARY AND CONCLUSIONS

This group of ovarian tumors has a distinct morphological background which, though subject to considerable variation, seems to differentiate them from other ovarian tumors. It would be a satisfaction if one could accept Schiller's theory of etiology. However, the characteristic pseudoglomerulus is so infrequently demonstrable that the linkage with the mesonephros is not possible with what is now known. The similarity of the acini to collecting duct tubules is insufficient to make this relationship convincing. It is important, however, for purposes of study as well as treatment to separate tumors into distinct cate-

gories when this can be done and we feel that this is justifiable in this instance.

The known facts seem to show that the tumor has many of the characteristics of the pseudomucinous and serous cystadenomas though it is neither of these for the well differentiated benign form has not the remotest resemblance to either. The fact that the tumor secretes mucinous material is significant and the finding of serous, granulosa, and thecal elements lead us to conclude that for the time being it would be better to regard the group as teratoid cystadenomas until more can be known about them.

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EXPERIMENTAL OBSERVATIONS ON RECONSTRUCTIVE INTRATHORACIC ESOPHAGOGASTRIC ANASTOMOSIS FOLLOWING RESECTION OF THE ESOPHAGUS FOR CARCINOMA

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CARCINOMA of the esophagus is rapidly assuming a more important position among the surgical entities. This recent progress has been demonstrated by the large number of successful transthoracic resections of carcinoma of the cardiac end of the stomach with re-establishment of the esophagogastric continuity which have been done. Until recently, these patients were refused operation as being hopeless. This progress has been made possible by a more thorough understanding of the physiology of the thorax, the refinement of surgical technique, and the progress that has been made in the field of anesthesia for major intrathoracic operations.

During the 10 year period, between 1931 to 1941, at the University Hospital, 185 patients have been seen with carcinoma of the esophagus. Approximately a quarter of the lesions in these cases occurred in each of the following situations: the upper one-third, the middle one-third, the lower one-third of the esophagus, and carcinoma of the cardiac end of the stomach infiltrating the esophagus secondarily. Twenty-five per cent of the patients with carcinoma of the esophagus coming to necropsy at the University Hospital had no evidence of metastases or extension of the carcinoma beyond the confines of the esophagus. Another 15 to 20 per cent had regional lymph node metastases alone. Consequently, one might assume that approximately 40 per cent of the patients coming to necropsy present operable lesions. This compares with the reports by Abel, who stated that 25 per cent of the fatal cases of carcinoma of the esophagus are operable. Ochsner and DeBakey presented a series of 1,025 patients with carcinoma of the esophagus observed at necropsy, of whom 40.7 per cent showed no evidence of metastases. Sauerbruch found that 35 per cent of 117 patients, in which the carcinoma was situated between the hilum and the cardia, died without forming distant metastases, and Starlinger found that 66 per cent of the cases examined had no metastases. Many patients die from either starvation, perforation of the carcinoma with resulting mediastinitis and empyema, aspiration pneumonia, or lung abscess.

The many obstacles in the progress of the surgical treatment of carcinoma of the esophagus have been stressed by Ochsner and De Bakey. One of the chief obstacles is the inherent anatomical characteristics of the esophagus. The esophagus has no serosal covering upon which the success of gastrointestinal anastomosis depends. It has a very meager blood supply and, consequently, great care must be exercised in preserving all the blood supply to the remaining esophagus. The main muscular coat is longitudinal and, consequently, tends to pull an anastomosis apart. The esophagus is relatively fixed and has no redundancy, making operative procedures difficult. Furthermore, carcinomas of the esophagus are located immediately adjacent to many vital structures, which make all operative procedures technically difficult. In addition to this anatomical background, patients with carcinoma of the esophagus usually present themselves in a dehydrated and malnourished or emaciated condition. They usually have avitaminoses with complications. Because of esophageal obstruction with stasis of food and mouth secretions, the bacterial flora are very virulent, and favor postoperative infections.

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Because, until recently, treatment of carcinoma of the esophagus has been so unsuccessful, the attention of the general practitioner has not been focused sharply enough upon the significance of dysphagia in the early diagnosis of this condition, and the importance of an early esophagoscopic examination has been widely neglected. It was shown in a comparative analysis of carcinoma of the gastrointestinal tract (5) that the smaller the caliber of the organ, the shorter the latent period, and the smaller the neoplasm before causing symptoms. The esophagus is a relatively small caliber organ and, therefore, a neoplasm should cause symptoms relatively early. Consequently, patients with carcinoma of the esophagus should present themselves for treatment much earlier than patients with carcinoma situated elsewhere in the gastrointestinal tract. Because of this, it is disheartening when patients present themselves with histories of dysphagia that has been present a year or longer. As surgical management improves, these patients will be referred for treatment earlier.

As to the disposal of the 185 patients with carcinoma of the esophagus seen in the last 10 years at the University Hospital, 51 patients, 27 per cent, were not treated. Many of these patients had no clinical evidence of metastases or inoperability that could be determined from examination of their records. Fifty-eight patients, 31.3 per cent, had only gastrostomies, with the appalling operative mortality of 45 per cent. The average length of life following gastrostomy was 4 months.

Forty-two patients, 22 per cent, had gastrostomy plus retrograde radium implantation. There was a 31 per cent mortality directly resulting from this procedure. Many of the deaths were due to traumatic perforation of the carcinomatous esophageal wall and subsequent mediastinitis and empyema. Other deaths were due to irradiation necrosis and subsequent mediastinitis. Still others died from the complications associated with the gastrostomy. Some of these patients also had supplementary irradiation therapy. This procedure was the procedure of choice from 1935 to 1938 and included the most favorable group of patients with regard to the likelihood of response to treatment. The length of life following treatment in this group was 4.8 months. Eighty per cent of these patients had no clinical evidence of metastases as determined by clinical examination, including exploration of the upper abdomen at the time of the gastrostomy. No cures were obtained in this group. Ten patients, 5.4 per cent, had irradiation therapy alone. Among this group, 1 patient is alive 3½ years following treatment. This was a patient having a lye stricture in which there is some doubt as to whether he actually had a carcinoma. During this 10 year period there have been 6 esophagectomies, with a mortality of 50 per cent, and 5 other thoracotomies in which the lesion was found to be inoperable. This mortality is lower than the mortality percentage reported by Ochsner and DeBakey in a series of 58 esophagectomies from the literature, which was 70.6 per cent. Within the past 6 months there have been 4 successful transpleural esophageal and gastric resections with esophagogastric anastomoses, and there has been no mortality. A fifth patient was found to be inoperable by this approach.

The technique of the transpleural partial gastric resection and resection of the distal end of the esophagus with esophagogastric anastomosis for carcinoma of the cardiac end of the stomach fulfills all the principles for a sound surgical operation, provided that enough of the stomach can be brought up into the chest to permit an anastomosis without tension following a sufficiently wide resection of the carcinoma. There is an excellent exposure. The regional lymph nodes can be included in the resection. Furthermore, the esophagogastric continuity is restored, so that the patient may eat normally and not be subjected to the disadvantages and the inconveniences of a gastrostomy for the remaining period of his life.

The Torek operation for carcinoma located elsewhere in the esophagus also allows wide resection of the carcinoma and of the regional lymph nodes, but it provides no means for reestablishment of the esophagogastric continuity. The cervical esophagostomy can be connected to the abdominal gastrostomy in 2 ways. The first is by a rubber tube. These rub-

ber tubes are an unending source of complaints. They frequently become dislodged from the esophagostomy or the gastrostomy opening and become plugged with débris. The second way of re-establishing a passageway between the esophagostomy and the gastrostomy is by means of an anterior thoracic esophagoplasty, utilizing skin tubes which are anastomosed to the esophageal stoma above, and either to the stomach, a gastric tube (Beck, Jianu), or a segment of jejunum below, which in turn may be anastomosed to the stomach.

These operations are difficult to perform, necessitate multiple operations with a high mortality, and function well afterward in only a small number of cases. In a collected series of cases of anterior dermatoesophagoplasties reported by Ochsner and Owens, an average of 4.5 operations per case with an operative mortality of 30 per cent was found. Of the entire group, 56.6 per cent of the esophagoplasties were never completed. The authors warned of the danger of digestion of the skin tube by gastric contents with consequent gangrene and fistula. In a series of 36 cases in which the jejunum was utilized in forming an anterior cutaneous jejunoesophagoplasty, there was a 46 per cent mortality; only 43.3 per cent of the cases were completed. The greatest complication in this group was interference with the circulation of the mobilized segment of jejunum, resulting in gangrene. In 70 cases in which jejunodermatoesophagoplasty was carried out, there was an average of 4.3 operations per patient, and a 22.7 per cent mortality. In 35 per cent of the patients, the operation was not completed.

Consequently, up to the present time, even though a patient may be freed of carcinoma of the esophagus by an esophagectomy, the likelihood of again swallowing satisfactorily is quite remote. Any procedure that could be devised to combine complete removal of the carcinoma of the esophagus with the regional lymph nodes, and allow re-establishment of the esophagogastric continuity, that did not necessitate a large number of operations for its completion, and did not have a prohibitive mortality, would certainly be a step forward in the surgical management of this disease. With this goal in mind, 3 series of animal experiments (in dogs) were carried out in an attempt to fulfill these requirements. This article is a preliminary report of these experiments.

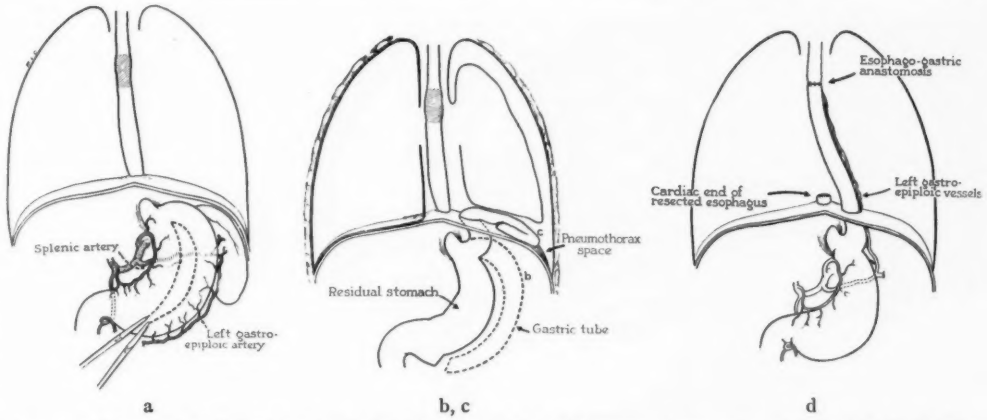
Experimental Data[1]

I. Reconstructive Intrathoracic Esophagogastric Anastomosis

In the first series of experiments the esophagogastric continuity was restored by the construction of a greater curvature gastric tube which was anastomosed to the proximal esophagus at a subsequent operation. The operation was divided into two stages. The first stage, performed through an abdominal incision, under drop ether anesthesia, consisted of fashioning a gastric tube from the greater curvature of the stomach similar to that described originally by Jianu, and lately by Carter and associates. The tube extends from about 5 centimeters proximal to the pylorus to within 3 or 4 centimeters from the cardiac orifice of the stomach. The tube was originally made by us by making a small opening through both the anterior and posterior walls of the stomach approximately 2.5 centimeters from the greater curvature. Two rows of curved hemostats were then applied, including both the anterior and posterior walls of the stomach within the jaws of the hemostats, and the stomach was then cut between the hemostats. The hemostats were then removed one by one from above downward, while a hemostatic layer of continuous No. 0 dulox suture was inserted. This was followed by a continuous inverting layer of sutures. An occasional interrupted silk suture was then used wherever reinforcement of the suture line was needed. By this technique, gastric tubes measuring 20 to 30 centimeters in length have been made. Both ends were left attached to the stomach so that the lumen of the tube communicated with that of the stomach. The spleen was removed in order to allow greater mobilization of the gastric tube at the second stage of the operation.

At the second stage, usually 2 weeks after the first, a thoracotomy was done under posi-

[1]Dr. Alfredo Cesanelli, Rosario, Argentina; Dr. Juan S. Netto, Asunción, Paraguay; and Mr. William Troy, Ann Arbor, Michigan, were most helpful in the performance of the experiments.



a b, c d

Fig. 1. a, Line drawing illustrating the construction of a long gastric tube from the greater curvature of the stomach. b and c, Line drawing illustrating the placing of the greater curvature gastric tube through a new diaphragmatic hiatus into a left pneumothorax space. d, Line drawing illustrating the formation of the esophagogastric anastomosis between the proximal end of the esophagus and the gastric tube.

tive pressure intratracheal ether anesthesia, the seventh rib on the left side being removed. The esophagus was partially resected, the lower end being inverted. An incision through the diaphragm was then made, beginning approximately 2 centimeters lateral to the esophageal hiatus and extending laterally along the course of the muscle fibers. The gastric tube was then transected at the pyloric end, the stomach closed, and the tube with its mesentery and the included gastroepiploic vessels brought up into the chest. The diaphragm was closed with interrupted sutures up to the new hiatus. At this location the diaphragm was sutured to the gastric tube in order to prevent subsequent herniation of the abdominal contents into the chest and in order to take tension off the tube. An end-to-end anastomosis was then made between the end of the esophagus and the gastric tube (Fig. 1d). The mediastinal pleura was sutured to the gastric tube over the anastomosis in order to re-enforce the suture line and to relieve tension. In many of the operations the gastric tube was sutured to the prevertebral fascia to relieve tension. This, however, was not always necessary, since the gastric tube was frequently redundant enough to relieve all tension. Five grams of sulfanilamide was placed about the anastomosis. The lungs were gently and slowly inflated by means of positive pressure anesthesia and the chest wall was closed. A urethral catheter connected to wall suction was left in the chest during closure in order to insure the complete evacuation of all the residual pneumothorax air.

During the second stage of this operation, certain disadvantages and technical difficulties were encountered. The first disadvantage was that during the 2 week interval between the first and second stages, frequently so many adhesions developed between the tube and the remaining stomach and adjacent structures that the freeing of the tube was technically very difficult and time consuming. The second disadvantage was that in order to have an adequate exposure for the abdominal part of the operation through a thoracic incision, a rib had to be removed (usually the seventh or eighth) which was much too low to give adequate exposure for making a high esophagogastric anastomosis, at which time it would be of advantage to have the fourth or fifth rib resected.

Consequently, the operation was modified so that, at the first stage, the greater curvature gastric tube was divided at the pyloric end (Fig. 1a). This end was carefully closed and the tube was examined to make sure that an adequate blood supply was present. A small opening was then made in the diaphragm, approximately 2 centimeters lateral to the esoph-

ageal hiatus, a left pneumothorax was obtained, and the gastric tube was placed in the left hemithorax as demonstrated in Figure 1b and c. Four interrupted sutures were then placed between the tube and diaphragm to hold the tube in place and to prevent other viscera from herniating into the chest. Care must be exercised not to close the hiatus too tightly, thereby impairing the circulation of the gastric tube.

With this modification, any desired rib may be resected at the second stage, since the abdomen is not reopened. The operating time was reduced as much as an hour or an hour and a half. Following resection of the esophagus, the gastric tube is readily available for anastomosis. Furthermore, with the fourth or fifth rib resected, the anastomoses could be made at a much higher level than originally, as is noted in the roentgenogram in Figure 2b, in which the anastomosis was just 2.5 centimeters below the apex of the left hemithorax. (Also see the gross specimen in Figure 2a in which the anastomosis is at the level of the arch of the aorta.) If, following resection of the esophagus at the second stage, the gastric tube is not long enough to be anastomosed to the esophagus without undue tension, the tube can be freed at the previously made diaphragmatic hiatus and additional tube, or even stomach, can be brought up into the chest.

Furthermore, the technique of performing the anastomosis was changed from the use of an inner continuous layer of catgut and an outer layer of interrupted silk, to two layers of interrupted silk. This was felt to give better apposition of the ends, less interference with the blood supply, and a more satisfactory anastomosis. Lately, because of the fact that the gastric tube has occasionally had a brawny ridge at its end where the tube had been sutured at the first stage, and because this ridge made inversion difficult during the performance of the end-to-end anastomosis, the anastomosis has been made between the end of the esophagus and the anterior aspect of the gastric tube approximately 2 centimeters from its end.

Complications. The number of difficulties experienced in experiments such as these upon dogs is tremendous. The important advantages of the facilities of a hospital and cooperation of the patient in the postoperative treatment were necessarily absent in the experimental work. Many of the difficulties encountered during the early part of the experiments were recognized and corrected. The operation is technically difficult. The operating time was originally long and the blood loss considerable. Several of the first dogs died of operative shock.

The mediastinum in dogs is very labile, consisting of only the two layers of mediastinal pleura in many places. Great care must be exercised to prevent a bilateral pneumothorax, which dogs tolerate extremely poorly. Postoperative pulmonary complications occur with considerable frequency and their treatment necessitates constant and conscientious care to prevent postoperative atelectasis, pneumonia, pleural effusion, pneumothorax, and empyema. Postoperative pulmonary complications (pleural effusion, atelectasis, and pneumonia) were the cause of death in 5 of the dogs during the early stages of the experimentation, before a very stringent postoperative regimen was instituted.

Because of the anatomical arrangement of the gastroepiploic vessels in dogs the amount of supporting tissue with the included vascular supply to the tube is considerably more bulky in dogs than in human beings. In the dog there are 3 or 4 left gastroepiploic vessels arranged in a fanshaped manner in relation to the greater curvature, in contrast to the human arrangement of one well defined left gastroepiploic vessel arising from the splenic, and running parallel to the greater curvature. Consequently, the gastric tube cannot be placed as high in the mediastinum in dogs as it can be in men because the pyloric end of the gastric tube can reach only as far as the length of the blood vessel to the pyloric end of the stomach permits. Furthermore, in bringing the gastric tube into the chest, it is necessary to transport a considerable amount of supporting omental tissue with the included vessels. This mass of tissue is an annoying source of exudate. Also, if this is too bulky, it frequently prevents complete re-expansion of the lung. In the one esophagogastric anastomosis

done in a man, the tube was the same width as the normal esophagus and was placed upon the esophageal aspect of the aorta. There was no protrusion of the tube into the hemithorax whatsoever. This operation was done entirely in one stage. This was at a time when the technical difficulties involved in leaving the gastric tube within the abdomen at the first stage of operation were realized, but before any experience had been obtained with placing the gastric tube within the chest at the first stage, as was done subsequently in the modification of the experimental technique. The esophagogastric anastomosis in this patient was made at the level of the aortic arch. Death occurred on the 12th day after operation as a result of a perforation of the anastomosis with subsequent mediastinitis and an encapsulated mediastinal empyema which had been inadequately drained.

The greatest difficulty encountered in dogs is the gastric acidity, which is about twice as high as that in a normal man. Because of this factor they tend to digest catgut sutures, unless given something to buffer the gastric acidity. This high acidity was felt to be the responsible factor in the cause of death in the only 3 dogs in which disruption of the anastomoses occurred. These dogs died on their 3d and 4th postoperative days. Necropsy examinations revealed practically no catgut sutures about the anastomoses. Furthermore, there was digestion of the terminal esophageal mucous membrane. This occurred during the period of experimentation when the dogs were not given anything to eat or drink after operation, but were maintained entirely on intravenous fluids for the first 3 or 4 days.

Postoperative treatment. Shock. As a result of the modification of the operative technique by which the gastric tube was placed within the chest at the first operation, the operative time was markedly reduced, and the blood loss decreased. Shock was not a troublesome factor from then on. Immediately following the operation and twice daily thereafter for 3 or 4 days, 200 cubic centimeters of 5 per cent glucose and 200 cubic centimeters of Ringer's solutions were given intravenously.

Pulmonary. Because of the tendency to pulmonary complications, a very stringent

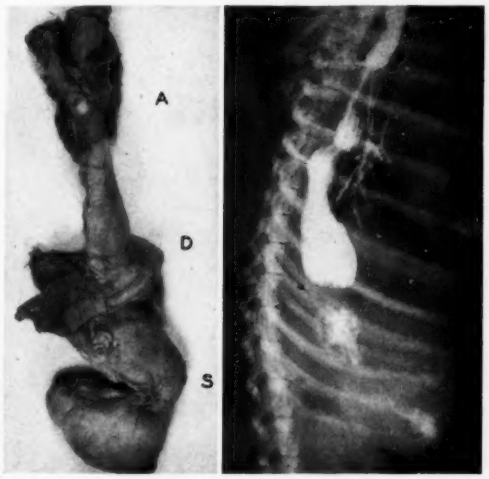


Fig. 2. a, left, Dog 12. Gross specimen of an esophagogastric anastomosis made at the level of the aortic arch. *A*, Anastomosis; *D*, diaphragm; *S*, residual stomach. b, Dog 13, postoperative roentgenogram of an esophagogastric anastomosis made 1½ inches below (upper arrow) the apex of the left hemithorax. Lower arrow indicates the new diaphragmatic hiatus. This had been made too small, with resulting partial obstruction.

regimen was instituted. This consisted of giving carbon dioxide inhalations every 2 hours until 11:00 o'clock at night for the first 2 or 3 postoperative days, in order to assure complete re-expansion of the lungs and to prevent postoperative atelectasis and pneumonia. Frequent examinations of the chest were necessary to detect the presence of fluid. If present, thoracentesis was done twice daily until fluid no longer formed. Each dog was given 2 or 3 grams of sulfanilamide daily for the first 3 or 4 days.

Gastric acidity. After the need to buffer the high gastric acidity that was present when the dogs were not fed was recognized, frequent small feedings were given every 4 hours for the first 6 postoperative days; these feedings consisted of 50 to 100 cubic centimeters of milk, 30 cubic centimeters of amphojel and 1/400 grain of atropine. After this regimen was instituted, there were no deaths as a result of disruption of the anastomosis.

Whereas the digestive factor in dogs is troublesome, this difficulty is not expected in human patients. Five of the last 6 patients with carcinoma of the esophagus seen at this

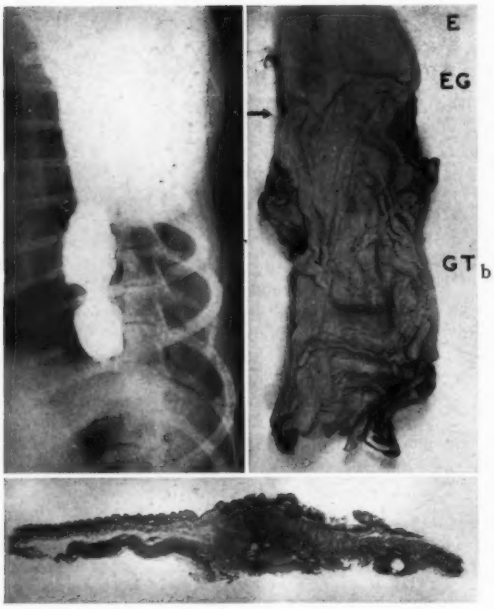
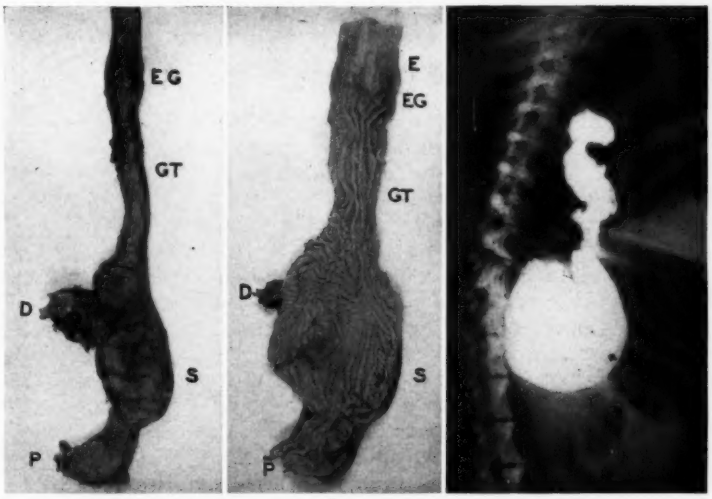


Fig. 3. a, Dog 10. Postoperative roentgenogram, 14 days, showing obstruction at diaphragm. Obstruction due to impacted sawdust in stomach. b, Gross specimen showing well healed esophagogastric anastomosis. *E*, Esophagus; *EG*, anastomosis; *GT*, gastric tube. c, Microscopical section of the esophagogastric anastomosis shown in Figure 3b, 15 days.

hospital during the past several months had no free hydrochloric acid in either the fasting specimen or after histamine injection; the sixth had no free hydrochloric acid in the fasting specimen, but did have following histamine injection. Though hydrochloric acid is not the only factor involved in digestion, it is an important index of the state of function of the gastric mucosa in such patients.

Results. A series of 12 dogs have had the complete operation. There were no deaths following the first stage of the operation, except perhaps one which might possibly be so considered. This dog (No. 13.) died just before the beginning of the second stage of the operation after he had been placed upon the operating table. This was 2 weeks after the first operation. The cause of death could not be definitely determined. However, several points of value were derived from this case. The gastric tube in this dog had been made very long so as to demonstrate the possibility of making an anastomosis in the very apex of the chest. Even though the dog had died, the anastomosis was performed, and the postoperative roentgenogram shown in Figure 2b was taken. The main point of interest derived from this dog was the fact that the end of the gastric tube had reopened. In spite of this, there was no evidence of pleural fluid or infection. It was felt that satisfactory healing had not taken place because the diaphragmatic hiatus had been closed too tightly and thereby caused partial impairment to the blood supply to the tube, with poor healing. The tightness of the diaphragmatic hiatus is demonstrated at the lower arrow in Figure 2b which shows obstruction to the passage of barium at the level of the diaphragm. Because of scar tissue contraction, the lumen of the hiatus will become smaller than that originally made. As a result of this observation, the second stage of the operation in which jejunal tubes were used (as described in part III) was performed after a shorter interval between the first and second stages, usually a period of 7 to 10 days. This was before scar tissue contraction had taken place. If the hiatus at the second stage was then found to be too tight, it was made larger.

All the remaining deaths occurred after the second stage. In only the last 4 of the 12 dogs was the operation performed in its final form that is, the tube was placed within the chest at the first stage and the present postoperative regimen followed. Three of the dogs lived sufficiently long to allow complete healing of the anastomosis. The fourth died on the fifth postoperative day from a perforated peptic ulcer which, as far as could be determined, had nothing to do with the operative procedure. The anastomosis in this dog, seen in Figure 2a, showed excellent healing and was functioning perfectly up to the time of death. One dog died on its tenth postoperative day, after having done very well, of a diaphragmatic hernia and pulmonary atelectasis. Another died on the fifteenth postoperative day from an overdose of morphine given at the beginning of an operation designed to relieve a supposed obstruction of the tube at the dia-



a b c

Fig. 4. Dog 11 sacrificed 14 weeks after operation. a, Photograph of gross specimen of esophagogastric anastomosis and gastric tube before opening. *EG*, Anastomosis; *GT*, gastric tube; *D*, diaphragm; *S*, residual stomach; *P*, pylorus. b, Same specimen photographed from within. *E*, Esophagus. c, Postoperative roentgenogram demonstrating widely patent anastomosis (upper arrow) and the propulsion of barium through the gastric tube into the stomach. Lower arrow indicates junction of gastric tube and residual stomach.

phragm as noted in the roentgenogram in Figure 3a. This dog had been eating both solid and soft foods very well until 2 or 3 days preceding death. Necropsy revealed that sawdust, which the dog had eaten from the floor of the cage, was impacted in the stomach and produced obstruction. The anastomosis was healed perfectly, as seen in Figure 3b and c. The fourth dog was sacrificed 14 weeks after operation. The dog had eaten very well, without vomiting. Postoperative fluoroscopic and roentgen examinations, Figure 4c, showed that barium by mouth passed readily from the esophagus through the tube into the stomach. Figures 4a and b are photographs of the gross specimen, which were made after this dog was sacrificed.

The results to date are certainly not conclusive but are suggestive of progress in the right direction. Many of the obstacles experienced at first have been overcome by subsequent modifications of the operative technique and particularly of the postoperative treatment. It has been gratifying to find that in only 3 of 12 cases has death been the result of disruption of the anastomosis. These disruptions occurred, not because of some technical error in performing the anastomoses, but as a result of the high gastric acidity and digestive action found in dogs. These deaths occurred during a time in the experimentation when the dogs were receiving nothing by mouth after operation to buffer the gastric acidity.

Physiological action of the gastric tube. The question arises, will these gastric tubes, which have been anastomosed to the esophagus in an antiperistaltic manner, function well enough to allow the patient to eat and maintain his weight? This can be answered only after more operations have been done, and the dogs observed over a long period of time. Dogs Nos. 9, 10, and 11, which lived for 10 days or more, were able to eat solid foods (canned dog foods) without vomiting if given in amounts not exceeding a tablespoon at a time. If the dogs were allowed to eat a larger quantity than this at one time they gulped the food, and vomiting was common. The physiological action of the gastric tubes was studied by fluoroscopy and

roentgenograms after barium was given by mouth. The barium would immediately shoot into the stomach as a result of the propulsive force of the pharynx. No evidence of peristaltic action was noted in any tube, in either the isoperistaltic or antiperistaltic direction. No difficulty is anticipated in the transportation of food from the esophagus into the stomach by means of the gastric tube because the pharynx has a strong propulsive action which tends to shoot the food through the tube, and the force of gravity tends to make the bolus drop to the stomach. Also, the fluctuating intrathoracic pressure tends to work with gravity in pumping the food into the stomach in case a large bolus is present. These views have been substantiated by studying this mechanism postoperatively by means of the fluoroscope. If strictures should develop at the anastomosis site, they could be dilated.

Clinical application. As to the clinical application of reconstructing an esophagus by a tube made from the greater curvature of the stomach, it is obvious that the stomach must be large enough for the construction of such a tube. Frequently, in patients with carcinoma of the esophagus, the stomach is small because of the inadequate filling of the stomach resulting from chronic obstruction of the esophagus. It is important that the size of the stomach be determined preoperatively by means of barium roentgenograms. If the stomach is small, and the patient can drink fluids, it can frequently be redilated by forcing fluids up to 4000 to 5000 cubic centimeters per day for 4 to 5 days preceding operation. By so doing, it has been possible in 3 patients to construct tubes 25 to 30 centimeters in length. If there is total esophageal obstruction, however, or if it is found impossible to redilate the stomach, then the operation is necessarily contraindicated.

If a suitable tube is to be constructed and mobilized in human beings, it is important, at the time of the first operation, to have adequate exposure at three points. These three points are at the pyloric end of the stomach, at the cardiac end of the stomach, and also in the left upper quadrant in order to allow splenectomy. The most satisfactory incision has been a midline incision extending from the ensiform cartilage to the umbilicus, and then laterally to the left costal margin. It is important that a splenectomy be done, because the spleen and the splenic vessels, are somewhat fixed to the posterior wall. If the spleen is not removed, adequate mobilization of the left gastroepiploic vessels, and in turn of the gastric tube, is not possible. If only a short gastric tube is needed, a splenectomy is not necessary. A jejunostomy at the first stage for feeding purposes should be considered.

If, at the second stage, the carcinoma is found to be inoperable, the gastric tube can either be (1) left alone, (2) brought out through the anterior angle of the incision as a gastrostomy, or (3), if the case warrants, a palliative anastomosis can be made by transecting the esophagus above the level of the neoplasm, inverting the distal end and anastomosing the proximal end to the gastric tube so that the patient can continue to eat and live a more comfortable existence during his remaining life. There is just as much justification for restoring the esophagogastric continuity in a patient suffering with carcinoma of the esophagus as there is in performing an ileocolostomy in a patient afflicted with carcinoma of the bowel.

SUMMARY

1. *Indications* for the construction of an intrathoracic esophagogastric anastomoses are: (a) a patient in good condition as to the state of nutrition, age and operative risk; (b) a patient who, barring complications, would have a relatively long life expectancy if the lesion is operable; (c) a patient who has only partial esophageal obstruction and whose stomach is large enough to construct such a gastric tube. This would allow the patient to eat after the first stage of the operation, and to maintain his nutrition before the second stage.

The *advantages* of the operation are: (a) probably the best method of re-establishment of the esophagogastric continuity and permitting all types of foods to be eaten; (b) accomplished in two operations, whereas the construction of an antethoracic cutaneous esophagoplasty requires multiple operations; (c) it is not disfiguring to the anterior chest; (d)

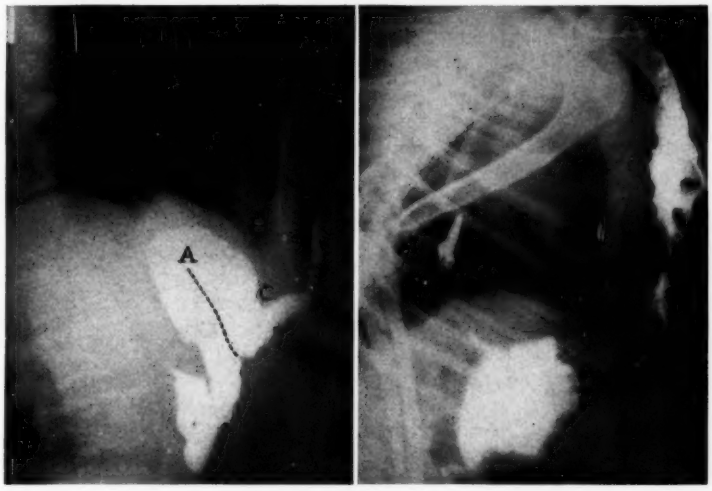


Fig. 5. a, left, Postoperative roentgenogram of a patient in which a greater curvature gastric tube was placed beneath the anterior thoracic skin almost to the level of the angle of Louis. *A*, Base of gastric tube at junction with cardia of stomach (shown in fluoroscopy but not in this particular projection); *B-C*, Position of three costal cartilages which might have been resected to decrease the distance from cardia of stomach to base of neck. b, Postoperative roentgenogram of an experimental antethoracic subcutaneous esophagoplasty carried out in one stage. Arrow points to site of anastomosis at level of manubrium.

following removal of the cancer, the gastric tube is immediately available for anastomosis; (e) an incision in the neck is not needed; (f) if the carcinoma is found to be irremovable, the gastric tube would permit a palliative sidetracking operation; (g) if, at the second stage of the operation, the gastric tube is found to be too short, the diaphragm can be reopened and additional tube and even cardia of stomach can be transported into the chest.

2. The *contraindications* are: (a) debilitated patients; (b) poor operative risks; (c) long continued or total esophageal obstruction in patients in whom the stomach would be too small to allow construction of a suitable gastric tube.

The *disadvantages* are that (a) a major operation is required before the surgeon knows whether the cancer can be removed; (b) the operation would probably be associated with a higher operative mortality than a Torek operation because of the risk associated with the intrathoracic anastomosis.

The performance of an intrathoracic esophagogastric anastomosis between the upper esophagus and a gastric tube made from the greater curvature of the stomach after resection of the esophagus for carcinoma appears to have certain merits if done in a selected group of patients. This group includes those patients who have only partial esophageal obstruction, who are still able to swallow enough food to prevent atrophy of the stomach so that a gastric tube of sufficient length may be constructed. This also allows the patient to eat between the first and second stages of the operation. Furthermore, the patient should present a good operative risk.

The final decision as to the type of operation to be performed depends on whether the surgeon is willing to accept the added risk of an intrathoracic anastomosis in order to secure for the patient a normal means of passing food into the stomach, rather than performing a Torek operation which requires gastrostomy feedings. The operative mortality of an esophagogastric anastomosis, using a gastric tube, would be no higher than a transthoracic esophagogastric anastomosis after resection of carcinoma at the cardiac end of the stomach. The

operative mortality would probably be higher than for a Torek operation, but much less than the combined operative mortality of a Torek operation and a later antethoracic cutaneous esophagoplasty. Experience alone can determine the feasibility of the operative procedures that have been illustrated by the experiments reported in this article.

II. RECONSTRUCTIVE ANTETHORACIC ESOPHAGOGASTRIC ANASTOMOSIS

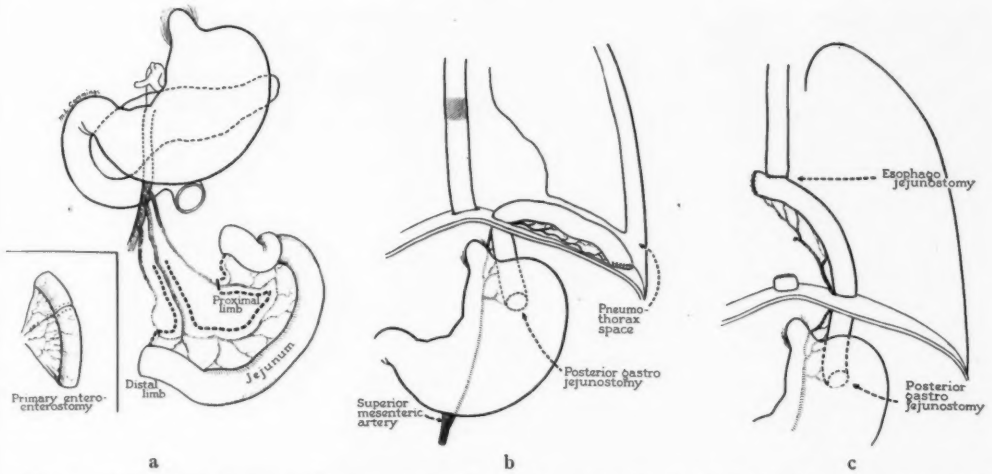
Many surgeons are of the opinion that the added risk of an intrathoracic esophagogastric anastomosis is not justified, and that an anterior esophagoplasty should be done. As a result of studying the postoperative roentgenogram (Fig. 5a) of a patient with a carcinoma of the esophagus in which a greater curvature gastric tube was constructed and brought out subcutaneously beneath the skin of the anterior chest wall, certain modifications of the operative technique were suggested which might be employed to increase the length of the tube, and consequently permit an anterior thoracic esophagoplasty to be done in one stage. The first modification was that the distance between the base of the tube at the cardia of the stomach, *A*, and the anterior chest wall might be shortened if the cardia of the stomach was placed directly beneath the costal cartilages. This can be done by incising the peritoneum and diaphragmatic peritoneal fascia about the esophageal hiatus in order to allow the lower thoracic esophagus to be pulled into the abdomen. This, in turn, will allow the cardiac aspect of the stomach and the base of the tube to lie just beneath the costal cartilages. The second modification was that a considerable length of tube was wasted by having to descend and then turn around the costal margin, *B-C*, before being tunneled beneath the anterior thoracic skin to ascend toward the neck. This angle may be greatly decreased by resecting the lower three costal cartilages just lateral to the sternum. It is necessary to remove the spleen in order to allow sufficient mobilization of the left gastroepiploic vessels.

With these modifications in mind, animal experimentation was done to determine the feasibility of such a procedure and to see whether it was anatomically possible. Only one dog was operated upon by the antethoracic esophagogastric anastomosis method but the procedure appears to have certain merits. Additional dogs were not operated upon because it is impossible to maintain a dog's nutrition by such a procedure. The increased distance to which this tube can be extended is illustrated by the postoperative roentgenogram (Fig. 5b), which illustrates the antethoracic esophagogastric anastomosis in a dog made at the level of the manubrium. In this particular dog, the cervical esophagus was transected at the level of the superior mediastinum. The distal esophagus was closed and dropped back into the posterior mediastinum. Following this, an end-to-end anastomosis was made between the upper end of the esophagus and the antethoracic gastric tube, and the cervical fascia and skin were then closed over it.

When the lower three costal cartilages are resected and when the diaphragm is pushed up or separated, it is important that the left hemithorax should not be entered. Opening of the pleura is less likely to occur in man because the mediastinum is wider than in dogs. If the pleural cavity is accidentally entered, the diaphragm should be sutured to the sides of the gastric tube to prevent herniation of the abdominal viscera into the thorax during the postoperative period.

There are at least three situations in which an antethoracic esophagogastric anastomosis appears feasible: (1) In patients having a highly situated neoplasm when there may be some doubt as to whether the upper esophagus could be reached for anastomosis with an intrathoracic gastric tube; if, after construction of the tube, the tube is too short for an antethoracic anastomosis, the remaining gap would have to be bridged by a skin tube; (2) patients for whom the added risks of an intrathoracic anastomosis would be unwise. (3) As a palliative measure in patients who have been found to have metastases or who are believed to be inoperable.

If possible, the antethoracic cervical esophagogastric anastomosis should be done at the same operation at which the gastric tube is formed, rather than creating a high thoracic



a b c

Fig. 6. a, Line drawing illustrating the construction of a jejunal tube to be anastomosed subsequently between the esophagus and stomach. b, Line drawing illustrating the formation of a posterior gastrojejunostomy and the placing of the proximal limb of the jejunal segment within a left pneumothorax space. c, Line drawing illustrating the manner in which an end-to-side esophagojejunostomy is formed.

gastrostomy at a first operative stage and the anastomosis at a second stage. The reason for this is the fact that when the gastrostomy end remains upon the skin surface for a period of several days it becomes edematous, brawny and secondarily infected and would then be relatively unsuitable for use in the formation of an anastomosis.

It is best to do a primary anastomosis between the gastric tube and the upper esophagus, the tissues of which are known to be compatible, rather than by using an intervening skin tube which tolerates gastric juice poorly. It is felt that an intrathoracic anastomosis would function better than an antethoracic anastomosis.

Since performing these experiments, it has been noted that Halpern in 1912 was successful in performing an antethoracic esophagoplasty in dogs by utilizing a greater curvature gastric tube.

III. RECONSTRUCTIVE INTRATHORACIC ESOPHAGOJEJUNOGASTRIC ANASTOMOSES

As was stated previously, in many patients having had long continued obstruction of the esophagus, the stomach is so small as to preclude the construction of a greater curvature gastric tube of adequate length and caliber. In such cases esophagogastric continuity may be re-established after resection of the diseased portion of the esophagus by the utilization of a segment of jejunum, as illustrated in the diagrammatic representations in Figure 6.

The jejunum has been employed previously by a number of investigators in antethoracic subcutaneous esophagoplasty, usually in conjunction with a skin tube (7). In the series of experiments to be described, a segment of jejunum was utilized for an intrathoracic anastomosis between the esophagus and the stomach. The operation was divided into two stages.

The first stage consisted of isolating a segment of jejunum approximately 18 to 24 centimeters in length. This segment was isolated in most of the experiments 3 to 4 feet below the ligament of Treitz. This distance was used because of the anatomical arrangement of the blood vessels in this area. The primary arches of the intestinal blood vessels are considerably larger here than elsewhere, and the distance between the primary and secondary arches is greater, and the arches run for a greater distance parallel to the intestine proper in this location than in the more proximal jejunum. Another reason for selecting a segment of jejunum 3 to 4 feet from the ligament of

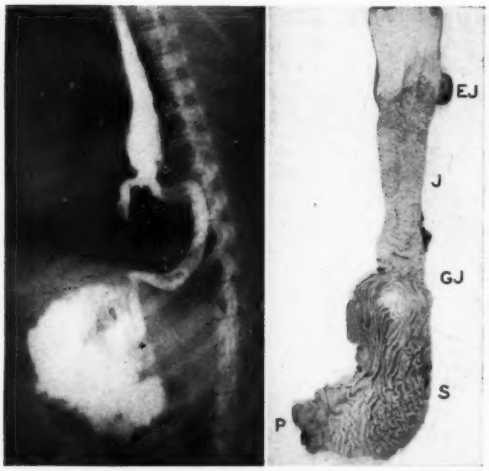


Fig. 7. a, left, Dog 3. Postoperative roentgenogram demonstrating good function of the esophagojejunostomy and gastrojejunostomy. (The esophagojejunostomy was made at the level of the upper arrow but after operation descended in the chest to the level of the middle arrow.) Lower arrow indicates position of the posterior gastrojejunostomy. b, Gross specimen, 10 weeks, demonstrating the jejunal tube anastomosed between the esophagus and the stomach as shown in the roentgenogram in, a. *EJ*, End-to-side esophagojejunostomy; *J*, jejunal tube; *GJ*, gastrojejunostomy; *S*, residual stomach; P, Pylorus.

Treitz is that the mesentery is longer in this region than it is higher, and it allows greater mobilization of the jejunal segment. Occasionally, a primary arch is sectioned proximal to its anastomosis with the adjacent arch in order to obtain a greater length of jejunal segment. A site is chosen in respect to the blood supply which will allow a long proximal limb to be placed in the chest in comparison with a shorter distal limb, that is to be anastomosed to the stomach. The mesentery is divided next to the vessels, as diagrammatically shown in Figure 6a, care being taken not to injure the vascular supply to that particular segment. The jejunum is then reunited by an end-to-end aseptic anastomosis.

The isolated jejunal segment with its blood supply is placed through a small opening in the transverse mesocolon into the lesser omental bursa. The distal end is anastomosed, Figure 6b, to the posterior aspect of the stomach approximately 3 to 4 centimeters below the esophageal hiatus, either by an end-to-side, or side-to-side anastomosis. The latter is better in dogs because of the small caliber of the jejunum. The longer proximal limb of the jejunal segment is then carefully inspected and, if the circulation appears adequate, the end is carefully closed with two layers of interrupted silk. If there are any color changes the impaired area is resected to normal tissue and the new end is closed. A small incision is made in the left diaphragm 2 centimeters lateral to the esophageal hiatus, and the long proximal limb of the jejunal segment is inserted into the pneumothorax space that was obtained in the left hemithorax when the diaphragm was opened. The jejunal tube is fastened to the new hiatus in the diaphragm by three to four interrupted sutures.

The second stage is performed in from 1 to 2 weeks, at which time the esophagus is partially resected and the upper end of the esophagus anastomosed in an isoperistaltic manner to the end or the side of the jejunum—the end-to-side anastomosis gives a larger stoma (Fig. 6c). The remainder of the operation is similar to that in which the gastric tube is used. The same postoperative treatment as used in the experiments with gastric tubes was employed in this series.

The one disadvantage of this procedure, in comparison with a gastric tube, is that the intrathoracic anastomosis must necessarily be at a lower level than that obtained with a gastric tube because a jejunal tube cannot be made as long as a gastric tube without impairing its blood supply. The intrathoracic anastomosis with a jejunal tube can be made at least as high as, or slightly higher than, the level of the hilum of the lung, whereas with the gastric tube method, the entire thoracic esophagus can be resected. In one dog, however, the esophagojejunal anastomosis was made at the level of the aortic arch, and further research may develop a technique by which a longer jejunal tube can be satisfactorily constructed.

Occasionally one is surprised at the second stage of the operation to find that a long tube has become considerably shortened as a result of disuse atrophy. The longest proximal limb of jejunal segment placed into the thorax in our experiments, so far, was 23 centimeters. From examinations of necropsy material, it appears

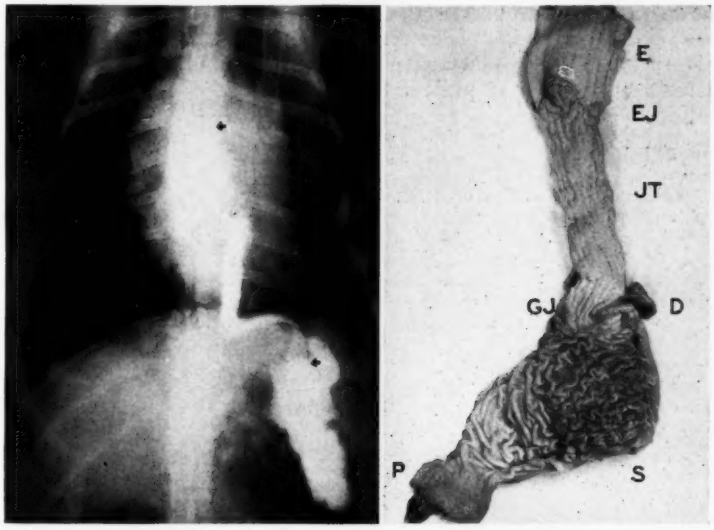


Fig. 8. a, left, Dog 5. Postoperative roentgenogram demonstrating the esophagojejunostomy just below the level of the aortic arch (upper arrow). Lower arrow indicates the position of the posterior gastrojejunostomy. b, gross specimen, 6 weeks, demonstrating the long jejunal tube anastomosed between the esophagus and stomach. *E*, Esophagus; *EJ*, end-to-side esophagojejunostomy; *JT*, jejunal tube; *D*, diaphragm; *GJ*, gastrojejunostomy; *S*, residual stomach; *P*, pylorus.

that a comparable length of jejunum can safely be isolated in human patients.

Results. Only 5 dogs have been operated upon according to this technique. There was only 1 operative death. This was on the ninth postoperative day as a result of an empyema. The necropsy examination showed the anastomosis to be well healed. All the remaining dogs lived and ate satisfactorily. One was sacrificed postoperatively because of pain from abdominal distention which was thought to be due to intestinal obstruction, but at necropsy was found to be the result of a hugely dilated stomach. Both the gastrojejunal and the esophagojejunal anastomoses in this dog showed perfect union. The other dogs were sacrificed 6, 10, and 12 weeks, respectively, after operation. All the gross specimens from these dogs showed excellent healing of the anastomoses and widely patent stomas. Figures 7 and 8 demonstrate the postoperative roentgenograms and the gross specimens of dogs No. 3 and No. 5 of this series. Fluoroscopic examination of these dogs revealed peristaltic action in the jejunal tube.

The inferior results obtained in the series of dogs in which a gastric tube was used, as compared with the series in which a jejunal tube was used, are explained by the fact that the jejunal series was the last series of dogs to be operated upon. By this time more experience had been obtained in the postoperative management of these cases.

Summary

A preliminary report, based upon animal experimentation, of operative techniques for the re-establishment of the esophagogastric continuity by intrathoracic and antethoracic anastomoses between the upper esophagus and gastric or jejunal tubes has been presented. This work is still in its initial stage and many more operations must be performed before conclusive results can be presented. If subsequent investigation proves that these techniques are of value, much progress will have been made in the surgical management of patients with carcinoma of the esophagus in restoring them to a state in which they can again enjoy the pleasures of eating. The ad-

vantages of the operative techniques described are that they provide for resection of the carcinoma and restoration of the esophagogastric continuity without subjecting the patient to multiple operations.

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GRANULAR CELL MYOBLASTOMA

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IN 1926 Abrikossoff first called attention to a peculiar tumor which he termed "myoblastic myoma" and which he thought was derived from striated muscle. It was considered to be a rare tumor until, in 1934, Klemperer reported 6 cases and collected 38 others from the literature. Since that time many additional reports have appeared under various names: myoblastoma (Klemperer), rhabdomyome granulo-cellulaire (Diss), rhabdomyoma and granular cell myoblastoma.

Gray and Gruenfeld again reviewed the literature in 1937, bringing the total of reported cases to 77, including 5 of their own. They tabulated the distribution of these neoplasms. The proximal part of the alimentary tract in general and the tongue in particular were the most common sites, although the tumors were widely distributed throughout the body. Table I reproduces Gray and Gruenfeld's list, with the addition of a number of subsequently reported cases and 30 tumors studied in the Laboratory of Surgical Pathology of Columbia University since 1909. This table does not include all of the reported cases of granular cell myoblastomas of the tongue, which have been recorded by Thoma.

The 30 examples studied in this laboratory include tumors arising in a wide variety of sites. Since tumors of this type in the middle ear and external auditory canal have not been previously reported, the data available concerning 2 cases occurring in this region encountered at the Presbyterian Hospital will be recorded.

CASE REPORTS

CASE 1. S.P. 43344, Unit Hist. 260291. R. M., a 60 year old white female, was admitted to the Ear, Nose and Throat service of the Presbyterian Hospital, New York, on June 26, 1930, complaining of intermittent bleeding from the ear over a period of more than 20 years. The lesion had been operated upon at least four times previously: first in Rumania shortly after the complaint developed. Examination revealed a large, smooth, pedunculated tumor filling the external auditory canal. It was removed in two pieces with a snare by the late Dr. Cornelius G. Coakley. Twenty-five months later, when the patient was last seen, there was no evidence of recurrence.

The specimen consisted of two resilient nodules of grayish white tissue showing areas of hemorrhage. They measured 1.5 by 1.0 by 1.0 centimeter and 1.3 by 0.5 by 0.5 centimeter, respectively. Histologically, the neoplasm was composed of closely packed, large, pale cells with granular, acidophilic cytoplasm and regular, relatively small, centrally placed nuclei. A delicate stroma, containing numerous capillaries, segregated the tumor cells into small rounded nests. Mitotic figures were not observed; nor were cross or longitudinal striations. With the Scharlach R stain no lipoid was demonstrable (Fig. 1).

CASE 2.[1] S.P. 82404, Unit Hist. 677455. E. R., a 77 year old white female, was admitted to the Ear, Nose and Throat service of the Presbyterian Hospital, New York, on June 15, 1942, complaining of a discharge from the right ear of 8 years' duration. Six years before, she had suffered a spontaneous facial paralysis with nystagmus. For 2 weeks the ear had been painful and bleeding. Other symptoms were deafness, dizziness, and difficulty with swallowing on the right side. Examination revealed a purulent discharge and a polypoid mass filling the external auditory canal. X-ray films demonstrated clouding in the mastoid region. A radical mastoidectomy was performed. Bleeding was copious and, because of it, the operator could not be certain whether the tumor arose from the middle ear or the external auditory canal.

The tumor was bilobed, the larger lobe measuring 1.5 by 0.7 by 0.6 centimeter. Part of the tumor was histologically a characteristic granular cell myoblastoma (Fig. 2). Other portions showed marked edema and were extremely vascular, the tumor cells being few in number and widely separated (Fig. 3). In these areas the cells showed a striking perivascular arrangement.

These two tumors appear to be characteristic granular cell myoblastomas. Although patient in Case 1 has been lost to follow-up after only 25 months, and patient in Case 2 has just been operated upon, the long dura-

From the Surgical Pathology Laboratory, College of Physicians and Surgeons, Columbia University, and the Department of Surgery, Presbyterian Hospital, New York.

[1]This case is reported with the permission of Dr. John D. Kernan.

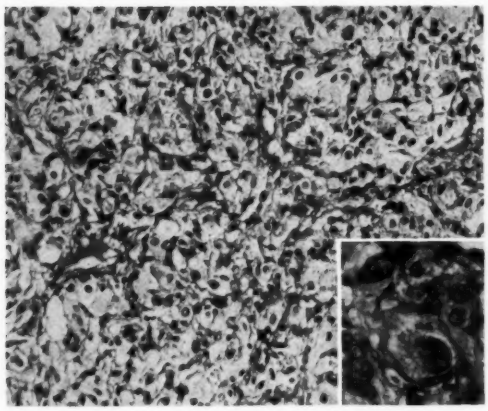

Fig. 1. Case 1. Granular cell myoblastoma of the external auditory canal. Hematoxylin and eosin stain. ×170. The section in the inset shows the granular character of the tumor cell cytoplasm. Masson's trichrome stain. ×490.

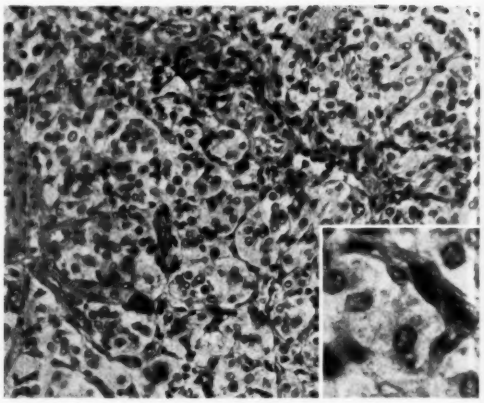

Fig. 2. Case 2. Granular cell myoblastoma of the external auditory canal. The tumor cells are arranged in a suggestive organoid pattern. Hematoxylin and eosin stain. ×170. The inset shows the characteristic granules. Masson's trichrome stain. ×490.

tions prior to operation are illustrative of the essentially benign nature of this type of neoplasm. Nevertheless, they may recur if incompletely excised, as indicated in the history of Case 1. This was observed in one other case in our series, that of Kernan and Cracovaner, with involvement of the vocal cord, which recurred 2 months after the first removal. However, the patient was followed for 2 years after the second operation with no further recurrence. There has been no evidence of malignancy in any of our 30 cases, but follow-up data are available in only 14. Of these, 1 patient died with nephritis shortly after excision of a subcutaneous myoblastoma of the back. The 13 other patients have been well and without evidence of recurrence for periods varying from 4 months to 9 years: 3 for more than 5½ years and 5 for from 2 to 4 years. A number of malignant tumors have been reported under the name myoblastoma, but it seems doubtful whether they should not be classified more properly as rhabdomyosarcomas. Von Meyenburg's case of "myoblastic sarcoma," included in Klemperer's series, is an example. It is described as showing atypical cells and numerous mitotic figures, findings which are not observed in what is generally accepted as the characteristic granular cell myoblastoma.

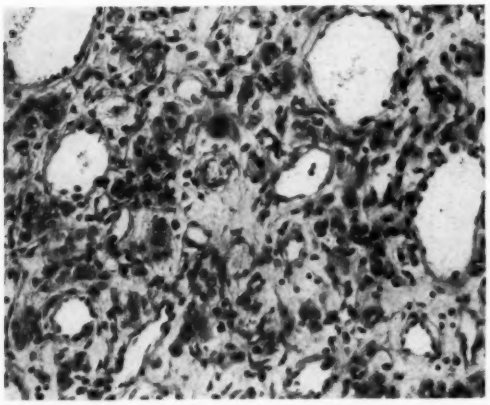

Fig. 3. Case 2. Granular cell myoblastoma of the external auditory canal. This portion of the tumor is highly vascular and contains few granular cells, which are widely separated and tend to be grouped about blood vessels. Hematoxylin and eosin stain. ×170.

Klemperer called attention to the active proliferation of the squamous epithelium overlying these tumors when they occur in the skin or just beneath a mucosal surface. This was present in 7 of our cases: 3 of the tongue, 2 of the vocal cord, and 1 each of the trachea and skin of the gluteal region. Several cases have been reported as examples of coincidental myoblastoma and squamous cell epithelioma. Indeed, in one of our cases the diagnosis of squamous cell epithelioma of the tongue was made in another hospital on biopsy, and ra-

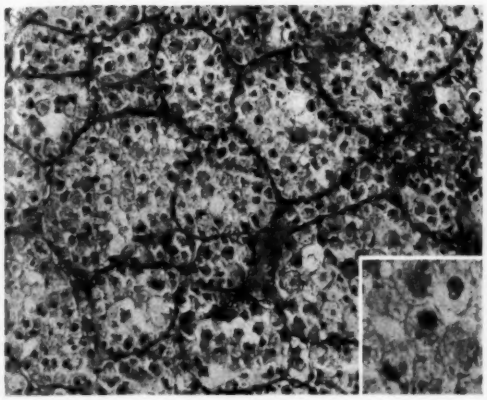

Fig. 4. Granular cell myoblastoma of the muscles of the thigh. The organoid arrangement of the granular cells in small nests, separated by a delicate, vascular stroma, simulates the appearance of endocrine gland neoplasms. Hematoxylin and eosin stain. ×135. In the inset cytoplasmic granules are few and small but distinct. Masson's trichrome stain. ×385.

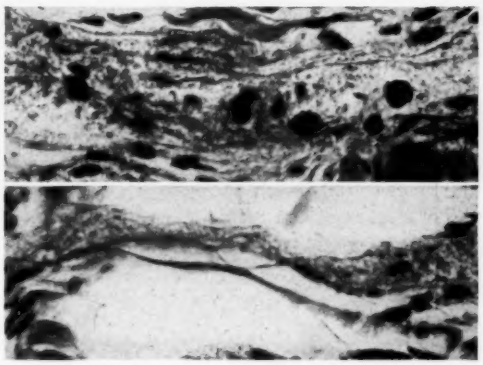

Fig. 5. Above. Granular cell myoblastoma of floor of mouth. The granular cell contains longitudinal striations suggesting myofibrils. Masson's trichrome stain. ×620.

Fig. 6. Below. Granular cell myoblastoma of the floor of the mouth. The ribbon-like cell shows parallel cross-striations at one end and, at the opposite end, numerous granules. Masson's trichrome stain. ×620.

dium treatment given before the patient came to this institution and the correct diagnosis of granular cell myoblastoma was established by excision. This case also provides evidence of the marked radioresistance of this type of neoplasm, since the tumor cells survived a sufficient dosage of radium to produce necrosis of the tongue.

In the tumors of this group there is great variation in the number, size, density, and depth of acidophilic staining of the characteristic granules. Paucity of granules in a given tumor may give rise to difficulties in diagnosis, especially when combined with an organoid pattern of growth which has been observed in a number of instances, including

TABLE I

	Tongue	Lip	Alveolar process of maxilla and mandible	Floor of mouth	Upper esophagus	Larynx and vocal cord	Trachea and bronchi	Skin	Subcutis	Muscles of extremities	Vulva	Breast	Orbit	External auditory canal	Total
Klemperer	21	1	6		1	4		7		2		2			44
Gray and Gruenfeld	13	1				4		2	3	6		4			33
Szathmáry											1				1
Frenckner	2	1				1	1								5
Von Bahr													1		1
Leroux and Delarue	2		1												3
Kramer							1								1
Tamis and Kowles											1				1
Grayzel and Friedman									1						1
Kratochvil			1												1
Authors'	5	1	2	1		1*	1	3	10	1		2		2	29*
	43	4	10	1	1	10	3	12	14	9	2	8	1	2	120

*One of the lesions in the Presbyterian Hospital series, a granular cell myoblastoma of the vocal cord, has been previously reported by Kernan and Crovaner and is included in Gray and Gruenfeld's summary.

Klemperer's 6th case and 4 of the cases in our series. Growths of this type show a striking perivascular arrangement of the granular cells with relation to numerous, thin-walled capillaries, simulating neoplasms arising from endocrine glands. Case 2 illustrates this organoid pattern of growth to some extent. It is much more striking, however, in two granular cell myoblastomas from the subcutaneous tissues of the arm and popliteal space, respectively, and in 1 from the muscles of the thigh (Fig. 4).

The histogenesis of the granular cell myoblastoma has not yet been definitely established, although most of the writers on the subject accept the theory of origin from myoblasts. This is suggested principally by the acidophilic cytoplasmic granules and the occurrence of ribbon-like syncytial masses. In addition, Abrikossoff and several later writers have described cross or longitudinal striations within granular cells or transitions between granular cells and striated muscle fibers. On the other hand, numerous observers have been unable to confirm these findings. Klemperer offers as explanation for this confusion the close proximity of granular cells and normal muscle fibers when these tumors infiltrate striated muscle, as they so frequently do. However, he also describes, in one of his cases, an arrangement of granules in parallel rows suggestive of striations. The general experience in this laboratory has been substantially in agreement with Klemperer. Only 12 of our 30 granular cell myoblastomas were distinctly encapsulated, the rest being infiltrating tumors. However, in the case of a typical myoblastoma occurring in the floor of the mouth of a 35 year old male, we have observed longitudinal striations suggestive of myofibrils (Fig. 5) and, in isolated granular cells, distinct parallel cross-striations (Fig. 6). Inasmuch as there is no striated muscle in the sections, there can be no doubt that these are tumor cells and not skeletal muscle cells. Therefore this observation appears as concrete evidence in support of the theory of the myogenous origin of these neoplasms. One other tumor, occurring in the subcutaneous tissues of the deltoid region, showed suggestive longitudinal striations and, in portions of scattered cells, a cross alinement of the granules without, however, distinct cross striations. In accepting the theory of the myogenous origin of the granular cell myoblastoma, one may suppose that the tumors occurring in sites where striated muscle is not normally present, arise from embryonal rests of aberrant myoblastic tissue. It does not seem necessary to believe, as Gray and Gruenfeld suggest, that these tumors are of myogenous origin in one situation and arise from some other tissue in other sites, since their appearance and behavior are identical in all locations, except when they assume the organoid pattern here described.

SUMMARY

Two cases of granular cell myoblastoma of the external auditory canal are reported and 30 cases of this type of neoplasm occurring in various body sites are reviewed. The finding of longitudinal and cross striations in an otherwise typical tumor of the floor of the mouth gives support to the generally accepted theory of the myogenous origin of these neoplasms. It is pointed out that some of the granular cell myoblastomas are highly vascular and have an organoid arrangement which may give them a resemblance to neoplasms of endocrine gland origin.

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HEMORRHAGIC INFARCT OF THE TESTICLE IN THE NEWBORN

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HEMORRHAGIC infarct of the testicle in the newborn has been recorded only once in the English literature (Campbell). In that case, the child was operated upon for tumor of the left testicle, at the age of 2 months. Dry hemorrhagic gangrene was found. Subsequently it was learned that at birth a diagnosis of bilateral hemorrhagic orchitis resulting from obstetrical trauma had been made.

We have had the unusual experience of seeing two cases of hemorrhagic infarct of the testicle within a 3 month period. Both cases were diagnosed during the first week of life, and the infants were operated upon on the fourteenth and tenth days of life, respectively.

CASE 1. Hospital No. B-17930, baby deB. was admitted to the hospital July 19, 1941. The mother was a trigravida secundipara. The first baby died at 6 months of age with diarrhea. The second pregnancy terminated in a self induced abortion. Kahn test of mother was negative. This was a normal pregnancy, full term, vertex presentation, delivered on July 19, 1941, without any difficulty and without instruments. The mother had a severe postpartum hemorrhage and went into collapse. A transfusion of 500 cubic centimeters of citrated blood was given. The mother recovered and convalescence thereafter was uneventful.

The infant was born with a mass in the left scrotal sac. Physical examination otherwise was normal. The temperature was normal, and the birth weight was 3,575 grams. The scrotum showed irregular areas of ecchymosis. The left side of the scrotum was markedly swollen, and contained a globular shaped mass measuring approximately 3½ by 2 centimeters in size. The mass was smooth and fibroelastic in consistency in contradistinction to the hardness associated with testicular tumor. The lower pole of the mass was adherent to the scrotum and did not transilluminate.

Laboratory examinations revealed: blood group, o; hemoglobin 17 grams; red blood cells, 5,800,000; white blood cells, 15,500; differential white blood cell count—polymorphonuclear leucocytes 27 per cent, lymphocytes 70 per cent, large monocytes 3 per cent; bleeding time, 4½ minutes; clotting time, 6½ minutes; urine examination, normal; Aschheim-Zondek test, negative; x-ray film of scrotum, noncontributory; x-ray film of chest, normal.

The child remained on the pediatric service under the supervision of Dr. Grover C. Powers. The child was breast fed. He was given hykinone 3.2 milligrams daily for the first 5 days after birth. A urological consultation was requested on the third day, and he was observed daily by the members of the urological staff for the next 11 days, during which time he gained weight to 3,600 grams on the eighth day of life, and then lost weight to 3,530 grams on the tenth day of life. During this period the child remained afebrile; the ecchymosis of the scrotum disappeared, but the size of the mass in the scrotum and the consistency of the mass remained unchanged. A diagnosis of hemorrhage into the left tunica vaginalis was made. On the fourteenth day of life, an exploration of the left side of the scrotum was carried out.

At operation an incision was made over the left external inguinal ring, extending downward and medially onto the upper part of the scrotum. The left cord was identified and freed. By blunt dissection the left testis and epididymis and tunica were freed and delivered through the wound. The tunica vaginalis was then punctured with a hypodermic needle, a few centimeters of bloody fluid being obtained. The tunica vaginalis was then opened from the upper to the lower pole of the testis. The tunica contained partly liquefied blood clots. The epididymis was found to be black in color, completely separated from the testis, and completely lacking in any blood supply. The testis itself was dark brown-red in color and appeared to have lost the greater proportion of its blood supply. Orchidectomy, left (complete), was carried out (Fig. 1).

The child developed an abscess in the left side of the scrotum on the eighth postoperative day. Aspiration of the abscess yielded 2 cubic centimeters of thick pus mixed with blood. On culture staphylococci were obtained. The upper angle of the wound was opened to provide adequate drainage. The child remained afebrile throughout this period and continued to gain weight from 3,530 grams on the day of operation to 3,800 grams on the tenth postoperative day. He was discharged from the hospital on the eighteenth postoperative day, completely well, and with the wound completely healed.

Pathology. The specimen consists of a membrane-like sac which has been partially opened, within which two hemorrhagic masses are noted. They are said to represent the tunica vaginalis, the contained epididymis, and the testicle. The spermatic cord is seen entering the tunica. The tunica itself is quite thickened, is red, and quite tough.

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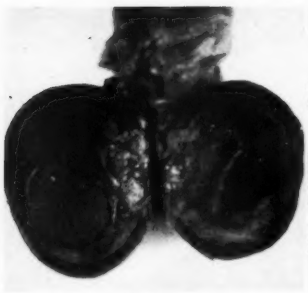

Fig. 1.

Fig. 1. Case 1. Photograph of surgical specimen, left testis, epididymis and cord, incised longitudinally, showing hemorrhage into testis, with tunica vaginalis filled with blood clot.

There is a folded fibrous band at the upper margin of the epididymis. The epididymis is an enlarged brown-red viscous mass, which is very friable. On section, the entire organ appears to be markedly congested with early signs of necrosis. The testicle as well is deep brown-red, quite soft and juicy, and tears readily. Sections were taken of the cord, the tunica, and the fibrous band, apex of the epididymis, the epididymis and of the testicle.

The sections of the testicle reveal almost complete necrosis of the entire organ, the central portion being replaced by fibrin, red blood cells, occasional polymorphonuclears, and necrotic débris. In some areas, remnants suggestive of seminiferous tubules are noted. Similarly in the sections taken through the epididymis there is marked necrosis and hemorrhagic infiltration of the entire section. Occasional tubules are noted which are recognized as such. In the section taken through the spermatic cord, the vas deferens is intact. The accompanying vessels are congested. There is no evidence of any thrombosis.

Diagnosis: Infarction of the left testicle and epididymis. L.L.W. (Figs. 2 and 3.)

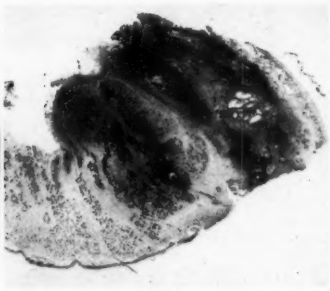

Fig. 2.

Fig. 2. Case 1. Photomicrograph of portion of testis, showing necrosis of central portion. ×5.

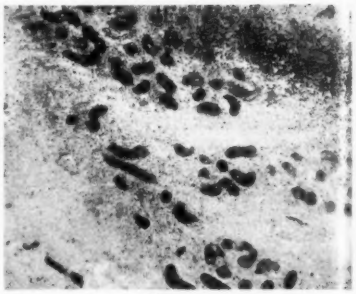

Fig. 3.

Fig. 3. Case 1. Photomicrograph showing degenerated tubules, with hemorrhage. ×40.

Case 2. Hospital No. B-21482, baby Fr. was admitted to hospital October 29, 1941. The mother was a quadrigravida tripara. This pregnancy was a normal full term pregnancy. The mother was delivered at home. Delivery was spontaneous, right occiput anterior, without instrumentation. The cord was around the baby's neck. The baby breathed with moderate stimulation, being cyanosed for only a short time. The birth weight was 9¾ pounds. At the time of delivery the scrotum was noted to be markedly edematous. It was thought that there was enlargement of the testicles.

On the third day of life, the baby was examined at home by the pediatric staff members in its regular follow-up of babies delivered on the outside obstetrical service. At this time, the whole scrotum was found to be edematous, and showed large areas of bluish-green discoloration, which had increased in size since birth. The left testicle was normal. In the right side of the scrotum, there was an egg shaped mass measuring approximately 2 by 3 centimeters. It was freely movable within the scrotum, and not adherent to it. The mass was stony hard in consis-

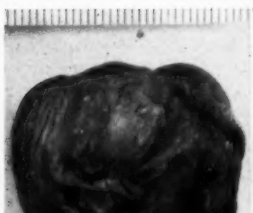

Fig. 4.

Fig. 4. Case 2. Photograph of surgical specimen showing discolored mass containing testis and tunica vaginalis.

Fig. 5.

Fig. 5. Case 2. Photomicrograph of testicle, showing tunica albuginea enclosing organized blood clot and complete degeneration of testicular tissue with adjacent epididymis infiltrated with blood. ×3.5.

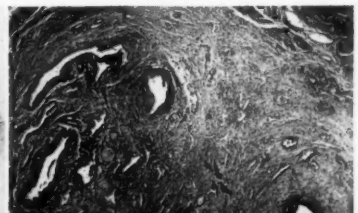

Fig. 6.

Fig. 6. Case 2. Photomicrograph of cord, with vessels which are free from thrombosis. ×20.

tency. Posteriorly, the epididymis could be differentiated from the testis in the upper portion only. The mass did not transilluminate. The right cord was thickened and firm. The child was admitted to the New Haven Hospital on the third day of life, on the pediatric service, under the supervision of Dr. Grover C. Powers.

Laboratory examinations revealed: Kahn test, negative; blood group A, hemoglobin, 18 grams; red blood cells, 5,160,000; white blood cells 9,850; differential white blood cell count—polymorphonuclear leucocytes 40 per cent, lymphocytes 46 per cent, large monocytes 9 per cent; blood platelets, normal; bleeding time, 1½ minutes; clotting time, 2¼ minutes; urine examination, normal; Aschheim-Zondek test, negative; x-ray of chest, normal, enlarged thymus noted.

A urological consultation was requested on the fourth day of life. The patient was observed daily by the members of the urological staff during the next 5 days, during which time the child remained afebrile. He was given formula feedings, and gained in weight from 4,600 grams to 4,700 grams. During this period the edema of the scrotum diminished; the areas of ecchymosis remained unchanged in size, but became deeper in color. The mass in the right side of the scrotum did not change in size or consistency. A diagnosis of hemorrhage into the right testicle was made. On the tenth day of life, exploration of the right scrotal sac was carried out.

A skin incision was made over the right external inguinal ring and extended downward, forward, and medially onto the upper portion of the scrotum. By blunt dissection the cord was freed, and the mass in the right side of the scrotum delivered into the wound. When the tunica vaginalis was opened, about 15 cubic centimeters of amber colored fluid escaped. Cultures were taken. These were later reported as showing no growth. The testis and epididymis appeared as a mass of grayish black necrotic tissue. Orchidectomy, right, and epididymectomy, right, were carried out. An elastic band was inserted as a drain through a stab wound in the dependant portion of the scrotum (Fig. 4).

Recovery was entirely uneventful, the child remaining afebrile throughout, and gaining in weight from 4,700 grams at the time of operation to 5,180 grams at the time of discharge on the fourteenth postoperative day.

Pathology. This specimen consists of the distal portion of a spermatic cord, the epididymis, testicle, and opened tunica vaginalis. At the junction of the spermatic cord in the epididymis there is a fusion of all the elements of the cord, and a rounded tight knot of soft tissue, the outermost coat of which consists of tunica vaginalis. There seems to be a natural constriction at this point. Distal to this, the tunica vaginalis is not remarkable. The testicle measures 4 centimeters in its longest diameter. When it is opened, it is seen to consist of a uniform deep brown colored tissue. The seminiferous tubules string with ease. Within the tunica albuginea, and distinct from the testicle, there is an encapsulated mass of soft tissue, which also appears to contain tubules. This is in no place continuous with the testicle proper. This too is of the same deep brown color as the testicle. The epididymis is present, and is not remarkable other than showing the uniform brown color. On cut section through the junction of the tunica vaginalis with the other elements of the cord, at the point of constriction, the vas is identifiable. The vessels are not distinct, but are fused together to form a uniformly brown tubular structure which apparently is thrombosed. This structure is about 3 centimeters in diameter. Representative sections were taken from the testicle, and the adjacent mass, as well as from the cord, for microscopic study.

In the sections of the testicle, a diffuse infarct is noted, involving all of the structures contained within the testicle, the epididymis, and its covering. There is evidence of old hemorrhage and beginning organization scattered throughout all portions on the slide. The epididymis is characterized by a similar process. In the section of the testicle, some of the vessels noted show evidence of calcium deposits within their walls. There is no evidence of any organizing thrombi. In the sections of the spermatic cord, the vessels are congested. There is no evidence of any obliteration of the lumina of these vessels. The spermatic cord and the vas deferens are present, and are not remarkable.

Diagnosis: Hemorrhagic infarct in right testis and epididymis, with beginning organization; calcium deposits within the intrinsic vessels of the spermatic cord. H.B. (Figs. 5 and 6.)

Hernia, hydrocele, epididymitis, tumor of the testicle, torsion of the testicle, and torsion of the appendix testis must be considered in the differential diagnosis of hemorrhagic infarct of the testis in the newborn. Hernia usually gives little difficulty in the diagnosis. It gives the characteristic impulse on coughing, is resonant on percussion, and when it contains bowel, gurgles on being reduced. A hydrocele has an elastic cystic feel to it, and transmits light. An acute epididymitis is invariably accompanied by severe pain and fever. There is no pain associated with hemorrhagic infarct of the testicle in the newborn, and the patient is afebrile.

Tumor of the testicle is nearly always stony hard in consistency. In these 2 cases of hemorrhagic infarct, the mass was stony hard in one, and fibroelastic in the other. In both cases, the ecchymosis in the scrotum provided sufficient evidence to eliminate tumor of the testis.

Torsion of the testicle and torsion of the appendix testis must be excluded. In both of

these, the onset of acute unilateral pain is practically always sudden. In torsion of the appendix testis there is a concomitant redness and edema of the scrotum at the onset of the attack, and in children there is a slight elevation of temperature. In cases of a few days' duration, unless edema persists, or a secondary hydrocele interferes, spot tenderness at the superior pole of the testis, and just under the globus major of the epididymis is diagnostic (Randall). In torsion of the testicle, Preen's sign is present. In hemorrhagic infarct of the testicle, the testicle can be palpated freely without the child showing any signs of discomfort. Figure 6 shows a cross section of the spermatic cord in Case 2. It will be seen that the vessels are entirely free from thrombosis.

A diagnosis is made by the presence at birth of a mass within the scrotum, the mass is usually egg shaped, and may be fibroelastic or stony hard in consistency; the presence of ecchymosis of the scrotum; and the absence of pain or tenderness in the affected testicle. Preen's sign is absent and the patient is afebrile. The white blood cell count may be slightly or moderately elevated, the red blood cell count remains normal.

CONCLUSIONS

1. Two cases of hemorrhagic infarct of the testicle in the newborn are presented.

2. In both cases the delivery was normal and uncomplicated.

3. A diagnosis is made by the presence at birth of a mass within the scrotum; the presence of ecchymosis of the scrotum; absence of pain; absence of Preen's sign; a normal temperature; and a slightly elevated white blood cell count.

4. Hernia, hydrocele, epididymitis, tumor of the testicle, torsion of the testicle, and torsion of the appendix testis must be considered in the differential diagnosis.

5. Torsion of the spermatic cord was not present in either case.

6. Orchidectomy was done in both cases, recovery being uneventful.

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THE IMMEDIATE EFFECTS OF 3,3′-METHYLENEBIS (4-HYDROXYCOUMARIN) ON EXPERIMENTAL ANIMALS

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IN a series of publications, Link and his associates (5, 9, 20) successfully showed the isolation, identification, and later synthesis of the hemorrhagic principle from spoiled sweet clover which has been responsible for the "sweet clover disease" of cattle (15, 16, 18). The substance is chemically 3,3′-methylenebis (4-hydroxycoumarin), and has the abbreviated name of dicumarol.[1] The economy of its manufacture by synthetic methods, the effectiveness by mouth, and the possibility of replacing heparin in preventing thrombosis, have attracted the attention of both experimental and clinical investigators. Published reports (1, 3, 4, 12, 21) indicate that in both animals and men, hypoprothrombinemia resulting from the administration of dicumarol requires a latent period of about a day. The peak of action may occur on the third day after a single dose. The prevention of the formation of thrombi can be demonstrated in dogs receiving dicumarol, thus providing the basis for clinical trials to prevent thrombosis (6, 14). A few preliminary papers on this point have appeared (7, 10, 11, 19, 22).

In animals which have succumbed to lethal doses, hemorrhage into various tissues and organs is an outstanding feature (3, 17). The liver of the rat is relatively more susceptible to dicumarol, often showing central necrosis after continuous administration (17). Dilatation of capillaries, small arteries, and veins has been observed in those animals that die acutely from massive doses (3). Other terminal effects, which have been recorded, include fever, dyspnea, coma (3) and convulsions (17). It is possible for dicumarol to kill animals within a few hours (17).

The purpose of the present communication is to report various results observed by us during the early stages of intoxication by dicumarol—prior to the onset of hypoprothrombinemia. In practically every experiment, a lethal dose was employed. The data deserve emphasis because they may not involve the same mechanism which determines the changes of prothrombin level.

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[1] Dicumarol is the collective trade-mark of the Wisconsin Alumni Research Foundation, which controls the use thereof.

METHODS

Dogs, rabbits, and albino rats were used in this study. The dogs were anesthetized with ether and the blood pressure was recorded from the carotid artery by means of a mercury manometer. Sodium citrate was employed to prevent coagulation of the blood in the arterial cannula. The respiration was recorded with a tambour connected to the side arm of the tracheal cannula. A 0.5 per cent solution of the disodium salt of dicumarol prepared according to Link's directions (private communication) was administered into the femoral vein. Before and after the dicumarol injections, the prothrombin time and the coagulation time were taken at intervals throughout each experiment. The individual doses injected ranged between 5 and 15 milligrams of dicumarol per kilogram of body weight.

For direct study of the behavior of the vascular system under the influence of dicumarol, albino rats anesthetized with ether or with pentobarbital sodium were used. Dicumarol in 0.5 per cent solution was injected into the femoral vein and its acute effects on the vascular bed were studied *in vivo* by the quartz rod transillumination technique. Precautions to prevent chilling of the animal were taken by placing the rat on a constant temperature platform (23).

The prothrombin time of diluted and undiluted plasma was determined by the Quick technique modified by Pohle and Stewart. A volume of 1.8 cubic centimeters of blood was

withdrawn into a syringe containing 0.2 cubic centimeter of 0.1 mol sodium oxalate solution, and then centrifuged.

The coagulation time was determined by the capillary tube method, and the red cell count made according to routine procedures.

RESULTS

The intravenous administration of 5 to 10 milligrams of dicumarol per kilogram of body weight in the form of a 0.5 per cent solution of dicumarol into anesthetized dogs brought about slight but transient fall in blood pressure and occasionally a slight increase in amplitude of respiration. However, when the total quantity administered amounted to between 40 and 60 milligrams of dicumarol per kilogram of body weight, the respiration became very rapid and irregular and was followed by severe dyspnea. In spite of the rapid and deep respiration, the blood became darker and darker as time went on. Cardiac irregularities, in the form of extra systoles, showed up in some of the animals. Hyperpyrexia became quite evident and the animal's temperature rose from an average of 38.5 degrees C. to as high as 42 degrees C. by the end of the experiment, which invariably lasted less than 1 hour. A generalized vasodilatation was manifested and the heart action and respiration stopped simultaneously resulting in death of the animal within 1 hour from the very start of the experiment. There was no change in the prothrombin or coagulation times throughout all the experiments. A slight rise of the red cell count was observed. Immediate postmortem examination showed a very dark and congested liver, an extremely contracted spleen, and very dark blood with general vasodilatation throughout the visceral and peripheral vessel beds. The onset of rigor mortis was immediate, and the animals became stiff soon after death. The findings under the influence of intravenously administered dicumarol may be summarized as follows:

(1) Rapid irregular respiration followed by severe dyspnea; (2) generalized vasodilatation; (3) extreme darkening of blood, in spite of rapid and deep respiration; (4) cardiac irregularities, extra systoles; (5) hyperglycemia; (6) hyperpyrexia—temperature rose from 38.5 degrees C. to 42 degrees C.; (7) hypermetabolism; (8) heart action and respiration stopped simultaneously; (9) liver very dark and congested; (10) spleen extremely contracted; (11) coagulation and prothrombin times did not change throughout the experiment; (12) slight hemoconcentration; (13) the animals became stiff immediately after death.

TABLE I.—LETHAL DOSES OF DICUMAROL IN ANESTHETIZED DOGS

Dog number	Intravenous dose mgm. per kgm.	Total amount administered mgm.	Results
1	45	382.5	Died after 31 minutes
2	55	412.5	Died after 33 minutes
3	40	680	Died after 25 minutes
4	55	687.5	Died after 45 minutes
5	60	780	Died after 55 minutes
6	40	300	Died after 30 minutes
7	40	380	Died after 41 minutes
Controls			
6a	34.66 c.c.	260 c.c.	No effect
7a	24.21 c.c.	230 c.c.	No effect

In order to determine whether or not any of the other ingredients of the dicumarol solution had any effect on the animals, control solutions were made incorporating all the ingredients exclusive of dicumarol. A total of 260 cubic centimeters of this control solution was given to one normal dog, and a total of 230 cubic centimeters to another. Neither of the control animals showed any toxic effects. It was justifiable, therefore, to conclude that the aforementioned manifestations were due to the dicumarol administered in the solution. Table I gives the dosages of dicumarol and of the control solutions per kilogram of body weight and per animal, and indicates their outcome. It should be noted that all the experimental dogs died within 1 hour and showed the findings as here listed, while the controls were not at all affected by a solution containing all the ingredients except dicumarol.

The *in vivo* study of the vascular bed in the anesthetized albino rat by the quartz rod transillumination technique demonstrated a generalized dilatation of the small vessels of the splanchnic area. No damage to vessel walls, however, could be observed.

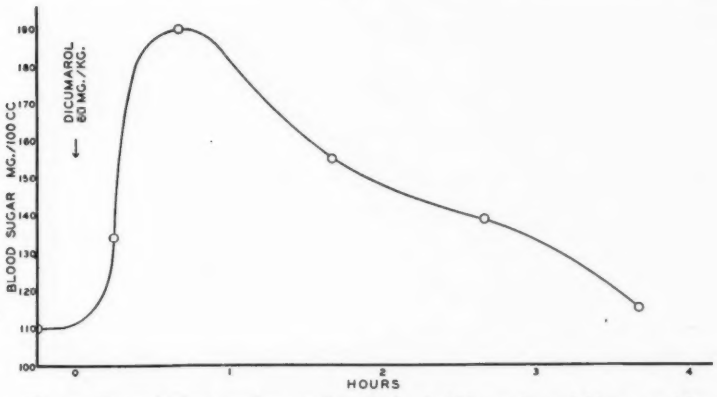

Fig. 1. Hyperglycemic action of dicumarol. Rabbit, male, weighing 2.13 kilograms, was given by the marginal ear vein dicumarol in the dose of 60 milligrams per kilogram. Note the rise of blood sugar from 110 to 190 milligrams per 100 cubic centimeters in 40 minutes.

Since hyperpyrexia was consistently observed in anesthetized dogs under the influence of intravenously administered dicumarol, we were interested in finding out whether or not it would raise the temperature of the conscious animal. Five trained dogs were used and every one developed hyperpyrexia when the drug was given intravenously in the dose of 50 to 60 milligrams per kilogram. We were further interested in finding out whether or not dicumarol would produce a rise of temperature in the rat when administered orally. A dose of 700 milligrams per kilogram was administered orally to a group of 4 rats; one of 900 milligrams per kilogram to another group of 5 rats; and one of 1000 milligrams per kilogram to a third group of 5 rats. Their rectal temperature was recorded hourly with a thermocouple and a definite rise of temperature was obtained.

In view of the hyperpyretic action of dicumarol, an acceleration of metabolism was suspected. Twelve rats were given dicumarol orally in the dose of 700 milligrams per kilogram, and their metabolic rates were measured in a Benedict's multiple chamber respiration apparatus (2). There was a uniform increase of metabolic rate: on the average, 119 per cent during the first hour after the medication, 202 per cent during the second hour, and 229 per cent during the third hour, as compared with the initial rate, namely, immediately before the medication. Five animals died before the end of the third hour.

To determine whether or not dicumarol has any effect on blood sugar, rabbits were given doses of 50 to 60 milligrams per kilogram intravenously. Their blood sugar was determined by the Hagedorn-Jensen method (8). There was definite evidence of hyperglycemia with prompt recovery. Figure 1 shows an example of the effect of intravenously administered dicumarol on the blood sugar of a rabbit.

ANALYSIS OF STUDY

Heretofore, dicumarol has been known to reduce, after a prolonged latent period, prothrombin levels of experimental animals. When the dose is excessive or frequently repeated, hypoprothrombinemia leads to severe hemorrhages and death. The results from the present investigation are interesting, particularly because they appeared promptly after the administration of dicumarol. It is probable that their occurrence is not associated with the same mechanism which controls the changes of prothrombin time. The sudden circulatory collapse in dogs suggests the acute dilatation of the capillaries and small vessels due to the drug, which has already been observed in the visceral organs. The direct action on the heart has not been excluded. The increase of metabolic rate and the rise in rectal tempera-

ture constitute another side action. Either circulatory collapse simulating shock, or hyperpyrexia may be the cause of the very acute death in animals. The brief hyperglycemic effect cannot be explained without further elaborate studies of carbohydrate metabolism under the influence of dicumarol.

It must be pointed out that the above results were observed with lethal doses in animals. They have no clinical application when therapeutic doses are employed in men. The only place where these toxic manifestations may be kept in mind is in cases of poisoning, accidental or otherwise, by unusually large amounts of dicumarol.

SUMMARY

1. Intravenous injection of lethal doses of dicumarol to anesthetized dogs results promptly in a series of toxic manifestations, including terminal circulatory collapse—without evidence of hypoprothrombinemia. No latent period of reaction is required.

2. Lethal doses of dicumarol injected intravenously to anesthetized rats cause splanchnic vasodilatation as shown by the quartz rod transillumination.

3. Hyperglycemia in rabbits, acceleration of metabolic rate in rats, and rise of rectal temperature in both dogs and rats, have been consistently observed shortly following the lethal doses of dicumarol.

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SIGNIFICANCE OF THE EXTENT OF AXILLARY METASTASES IN CARCINOMA OF THE FEMALE BREAST

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THE most important factor in predicting the survival of patients with carcinoma of the female breast after operative treatment has proved to be the presence or absence of metastases to lymph nodes in the axilla. However, little attention has been paid to the significance of the degree of lymph node involvement.

The fate of the patient obviously hangs on the complete removal of the cancer so that the condition of the axillary nodes already removed at operation does not have a direct bearing on the prognosis of a given patient. The cancer, if any, which remains behind is that which ultimately causes death. Moreover, hematogenous spread, fortunately uncommon in breast cancer, may have taken place, rendering the study of the lymph nodes worthless.

Despite these limitations, it is generally agreed that the 5 year curability by surgery of operable cases in which the disease is limited to the breast is about 70 per cent, while that of the operable cases in which there are metastases to lymph nodes is about 23 per cent. So far it has been customary to note the presence or absence of lymph node metastases without determining the number of nodes involved.

In an effort to exploit further the prognostic value of pathological examination we have studied a group of pathologically proved operable cases of carcinoma of the female breast in which the number of removed axillary lymph nodes involved by metastatic carcinoma was known. We would emphasize that this study does not refer to nodes believed to be tumorous by clinical examination. Taylor and Bruce, studying a group of cases which include most of the present series, found the discrepancy between clinical and pathological findings may introduce an error of 28 per cent. They stress the danger of giving too much weight to the clinical estimate of axillary involvement in planning appropriate treatment.

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MATERIAL

The 171 patients were selected on the basis of available pathological material from those treated at the Pondville Hospital from 1927 to 1936, inclusive. The bulk of them were those on whom radical amputation of the breast with removal of axillary lymph nodes was performed in that hospital. A few patients had had simple mastectomy or excision of a carcinoma performed elsewhere and had then been referred to Pondville for radical operation after a period of from a few weeks to 2 years. Some patients had received roentgen therapy, most had not.

The technique of operation has remained essentially the same in this period of time. The operators were members of the attending and resident staff, about 30 individuals in all. The criteria of operability were those in common use, namely, a movable primary tumor and freedom from metastases (except to the axilla) as far as physical examination and roentgenograms of the skeleton and chest can determine.

Several factors entered into the selection of the cases and the expression of the results that make this series unusual. Our primary interest has been the study of the natural history of the cancer so that some categories of cases are dealt with in an unconventional manner. For example, we have excluded operative deaths as inconclusive, because the time elapsed between the operation and death is often insufficient for metastases to become

TABLE I.—EFFECT OF EXTENT OF AXILLARY METASTASES ON SURVIVAL

	No. cases	Living and well 5 years Per cent	Living and well 5–13 years Per cent	Average survival cases dead with disease No. years
No metastases to axillary lymph nodes	81	85	76	4.7
Metastases involving less than half the axillary lymph nodes	22	68	50	4.6
Metastases involving more than half the axillary lymph nodes	31	38	22	3.4
Metastases involving all the axillary lymph nodes	37	19	16	2.2
Total with metastases to axillary lymph nodes	90	38	28	3
Total	171	60	50	3.3

evident. On the other hand, we have included 1 patient as a cure, who died only 4 years after operation, because autopsy failed to reveal any evidence of cancer. Ten patients were called cures at the time of death from intercurrent disease 6 to 10 years after operation because they had been observed by us frequently during the course of that time and had remained free of cancer. Nine of these were aged; the tenth, a 26 year old woman, died of rheumatic heart disease 7 years after operation and was found to be free of tumor at autopsy. Patients living with recurrences at the time of this study were included as dead. Otherwise the results are expressed in terms of 5 to 13 year survival free of disease on clinical examination. In this respect it is comparable rather to Simmons' series than to the conventional "5 year cure." In Table I, 5 year cures are also tabulated for comparison.

A fairly large number of cases was not considered suitable for study because the axillary contents had been lost or we had reason to believe that not all the axillary lymph nodes had been prepared for histological examination. This group occurred chiefly in the early years of the hospital before there was a standard procedure for examining the axillary contents.

The primary tumors were classified according to their microscopic characteristics as carcinoma simplex, adenocarcinoma, and mucinous carcinoma. Histological grading of carcinoma of the breast has not been found significant in this laboratory. The axillary contents were carefully examined and all the lymph nodes found were studied histologically. Coller has shown that by clearing techniques a substantially greater number of lymph nodes are discovered than by the usual methods and that metastases occasionally occur in the small, easily overlooked nodes. We have used only careful dissection and palpation of the axillary tissues.

One might question the validity of dealing with the number or percentage of involved nodes as we have done without knowing their relative positions in the axilla. This criticism is somewhat offset by the fact that a group without metastatic nodes or a group with all the nodes tumorous would be unaffected by any such means of classification. In our series only a single section was prepared of a given lymph node in most instances. While we realize that clearing techniques, serial sectioning, and the keying of nodes of basal, middle, and apical axillary groups might give more accurate data, these methods are time consuming, expensive, and generally unsuited to routine laboratory use. The method we have used is feasible in any pathology laboratory and as such has its advantages.

RESULTS

Effect of extent of axillary metastases. The 171 patients are divisible into four groups, namely, without lymph node metastases, with metastases involving less than half the lymph nodes, with metastases involving more than half the lymph nodes, and with metastases involving all the lymph nodes. Further subdivision is possible and gives results in keeping with the general trend, but the groups are too small to be of statistical significance.

The most significant finding is that curability on the basis of "5 year cure" or longer periods of observation is inversely proportional to the extent of metastasis in the axilla (Table I). Fifty per cent cure in the group with least axillary involvement and 16 per cent cure in the group with most axillary involvement varies significantly from the average cure rate of 28 per cent for the whole group with axillary metastases. The time of

survival in the fatal cases is also longer in the less involved group than in those more heavily involved. It is apparent, therefore, that the consideration of the whole group as homogeneous is ill advised. This is especially important to consider when small series such as this are studied for the purpose of judging the operation of some variable. An example of this will be dealt with later in this paper under the subject of recurrences in the operative scar.

The poor prognosis generally given the case with a few axillary metastases is probably unjustified. Although our data are insufficient to establish the point, we have gained the impression that patients with metastases to only one or two of a dozen or so axillary lymph nodes have nearly as great a chance of cure as those without such metastases. Moreover, patients with most or all of their axillary nodes involved by tumor not only have a much poorer prognosis for life but survive a shorter period than do those with less extensive metastases. The data on survival of the various groups are shown in Table I and are presented graphically in Figure 1.

The periods of time elapsed between operation and death in those who died of cancer in this series give further data. Seventy-seven per cent of those with all their lymph nodes involved were dead in 2 years whereas only 20 per cent of those with less than half their nodes involved died in a similar time. In the group without axillary node metastases we found, as did Simmons, that the patients who survived 5 years without recurrence may be considered permanent cures.

Effect of type of primary carcinoma. Mucinous (gelatinous or colloid) carcinoma or adenocarcinoma with mucinous foci was encountered in 5 patients in this series. Four showed no lymph node metastases, 1 had metastases to a third of the axillary nodes, which fact placed her in the lowest division of cases with lymph node involvement. All 5 of these patients are cured.

Carcinoma originating in papillary cystadenoma occurred in 7 patients. Six of these had no axillary metastases, 4 are cured. The seventh had all her axillary nodes involved and she is dead of cancer.

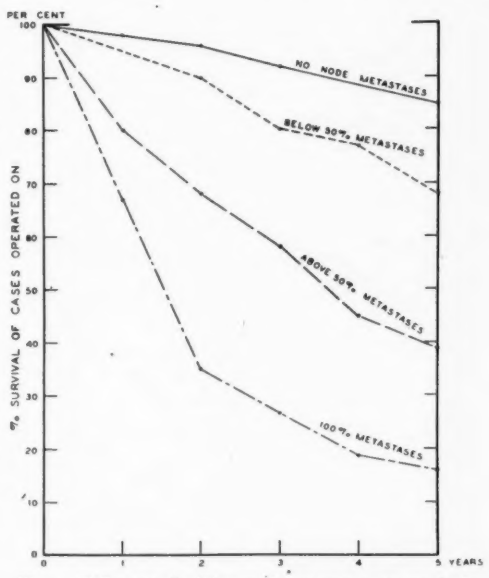

Fig. 1. Influence of axillary node metastases on survival.

Paget's disease of the nipple occurred in 4 patients. Three with metastases to lymph nodes are dead; the fourth with no lymph node metastasis is cured.

Adenocarcinoma occurred without lymph node metastases in 11 patients. Eight of these are cured. Four patients with the same type of tumor had node metastases and 2 of these are cured.

The majority of the tumors were classified as carcinoma simplex, and in these the results parallel the figures of the groups as a whole.

This is a small series on which to base conclusions, but it would seem that the type of tumor has less significance in prognosis than its extent.

We made no effort to grade the primary tumors according to the method of Broders. We do not ordinarily grade breast cancers because we believe the personal equation in the process to be very great, particularly as regards the intermediate grades, and we have found the results not significant. Variation in the grade of malignancy of these cases may account for some of our case distribution as regards metastases but cannot invalidate our principal conclusions.

TABLE II.—RELATION OF LYMPH NODE METASTASES TO RECURRENCES IN THE OPERATIVE SCAR

Number of cases	Metastases to axillary lymph nodes Per cent	Recurrences in operative scar Per cent
81	0	7
22	under 50	9
31	over 50	19
37	100	21

Recurrences in the operative scar. The data bearing on this point are presented in Table II. It is apparent that for this series at least, recurrences in the operative scar increase with the extent of the disease in the axillary lymph nodes. It is reasonable to suppose that patients in whom metastases have occurred to axillary nodes should also have other metastases to the skin or the chest wall, thus increasing the likelihood of recurrence in the scar. We believe the data support this supposition. The grave prognostic significance of such recurrences is seen in the group of patients in whom the lymph nodes were uninvolved. All the patients in this group who developed recurrences in the operative scar died of cancer. Of the 19 patients in the same group who died of cancer, 6 developed recurrences in the operative scar. In the group with axillary metastases only 2 of the 16 patients with recurrences in the scar were cured.

The incidence of recurrences in operative scars suggests that they are of the nature of metastases or extensions rather than implants. We believe that the variation of this type of recurrence in the reported series may be explained by differences in the type of cases treated and that this ought to be taken into account before deciding on the effect of changes or improvements in surgical technique.

SUMMARY AND CONCLUSIONS

The extent of involvement of axillary lymph nodes was studied in 171 cases of carcinoma of the female breast treated by radical mastectomy. Curability, as well as the survival time of patients not cured, decreases as the extent of metastases to the axillary lymph nodes increases. Recurrence in the operative scar is more apt to occur as the extent of axillary involvement increases.

Patients with metastases to the axillary lymph nodes do not form a homogeneous group, and there is prognostic value in further subdividing them. With such subdivisions the study of cases is made more accurate, even in small series, and the prognosis in a given case can be made with a little more assurance.

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"SHOCK" AND ANESTHESIA IN TRANSTHORACIC GASTRIC SURGERY

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THE point of view has persisted generally that only the robust are likely to withstand transpleural surgery. What truth there may be in this generalization remains to be shown; however, at this time enough material is at hand to permit an objective test of the matter, although of course the conclusions reached must remain tentative until a large body of material accumulates. Good material for examination in poor risk patients can be found in the group of patients who have carcinoma of the stomach. This lesion, approached by transabdominal wall route as well as by transpleural route for anatomical reasons, has now been operated on enough times[1] through the latter entrance to permit study and comparison of the shock producing effects of the two approaches. The material considered here is divided as follows: 64 patients with resectable carcinoma of the stomach have been studied; 17 of these have undergone gastric resection through the pleura and 17 by the traditional route; both of these groups were under ether anesthesia, and for comparison 30 patients have had gastric resection under spinal or splanchnic block or local anesthesia through the latter route.

From present experience it seems clear that the transpleural approach may in fact produce no more shock and perhaps even less than the transabdominal wall approach to the stomach. Thus, in addition to compelling anatomical reasons for approaching certain upper abdominal lesions through the thorax, the surgeon may be supported by a further fact: The excellent operative tolerance of the patient for the transpleural approach.

The principles and procedures of anesthesia which are important in transpleural abdominal surgery will be discussed, and in this connection probable reasons for the excellent tolerance of patients for the transpleural approach to the upper abdomen will be considered. And finally to be discussed are some lessons that have been learned from civilian thoracic surgery and anesthesia that are of importance in the care of war injuries of the chest.

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[1]Various writers. See most recently Churchill, E. D., and Sweet, R. H. (5).

MATERIAL AND METHOD OF STUDY

The material for this study was drawn entirely from the clinic. The problem has been approached chiefly through examination of the circulatory effects of the two routes of approach. It has been demonstrated that careful observation of the trend of the patient's systolic and diastolic blood pressure, pulse rate and quality, the skin circulation rate and skin temperature, blood color, and in some cases type and rate of respiration is useful in estimating the status of a patient at any given time and in predicting his course during operation. When one couples with these simple observations further objective data concerning the patients' circulatory stability during the immediate postoperative period and the character and duration of his recovery period in general, it becomes possible to state with considerable certainty whether one procedure is tolerated on the average as well or better than another. These matters are routinely followed in this clinic and notes are made concerning them. The patients of the two groups receive equivalent care, transfusions when needed, and oxygen.

For brevity, specific data (Table I) are presented concerning only systolic and diastolic pressures and pulse rate, since in these patients breathing oxygen-rich atmospheres[2] with adequate respiratory minute volume the other factors mentioned were satisfactory unless the contrary is specifically stated. In Table II the circulatory effects observed under the five methods of anesthesia customarily used for anesthesia in this hospital for gastric resection are recorded, the same number of cases being considered in the average for each group.

ANALYSIS OF STUDY

While the average data with the standard errors of the mean (Table I) give a good over-all picture, additional information is important. In the case of the transabdominal wall surgery (ether) only 1 (53 years of age) patient's systolic blood pressure

[2]It is possible to administer more than 95 per cent oxygen with ether. Under these circumstances the arterial blood oxygen remains normal during prolonged open pleura operations. For example, in 18 consecutive pulmonary lobectomies, Beecher and Murphy (unpublished data) have found that the arterial oxygen content was invariably normal.

TABLE I.—THIRTY-FOUR GASTRIC RESECTIONS FOR CARCINOMA UNDER ETHER ANESTHESIA
Averages with Standard Errors of the Mean

SEVENTEEN CONSECUTIVE TRANSABDOMINAL WALL APPROACHES

Age 54.0±3.0 Sex: 13M, 4F, Duration of procedure: 3 hours, 11 minutes ±8 minutes

	At entry to hospital	After 1 hour of anesthesia and operation	After 2 hours of anesthesia and operation	After 3 hours of anesthesia and operation
Blood pressure and pulse rate	Systolic 132.6±5.0 Diastolic 82.4±2.8 Pulse	125.0±7.4 72.3±3.9 104.5±3.8	128.2±6.1 80.0±4.7 103.3±3.0	118.7±6.0 72.7±3.7 103.4±3.5

SEVENTEEN CONSECUTIVE TRANSPLEURAL APPROACHES

Age 53.1±2.3 Sex: 14M, 3F, Duration of procedure: 4 hours, 11 minutes ±8 minutes

	At entry to hospital	After 1 hour of anesthesia and operation	After 2 hours of anesthesia and operation	After 3 hours of anesthesia and operation	After 4 hours of anesthesia and operation
Blood pressure and pulse rate	Systolic 118.3±3.2 Diastolic 72.0±2.4 Pulse 113.8±4.9	113.8±4.9 73.1±3.3 102.4±3.5	114.3±4.5 74.7±2.3 108.6±3.3	109.6±4.6 73.1±3.1 109.0±3.0	106.2±5.8 71.3±3.4 108.1±3.1

fell below 80 millimeters mercury. In this case the blood pressure had declined to 65/40 with a pulse rate of 120 at the end of operation, 2 hours and 50 minutes after the beginning of anesthesia. The patient was described as in poor condition with considerable surgical shock.

In the case of the transpleural surgery (ether), the blood pressure of 1 patient (68 years of age) slowly and gradually declined and at the end of operation, 3 hours and 50 minutes after anesthesia had started, had fallen to 78/50, with a pulse rate of 120. Other signs of shock did not develop and the patient was described as standing the operation well. Immediately following operation the blood pressure rose to 92/60 and then rapidly returned to normal. Another patient (36 years of age) showed a steady, gradual decline of blood pressure to 73/40, with pulse rate of 125, at the end of operation 4 hours and 10 minutes after the start of anesthesia. Other signs of shock did not develop. By the end of 1 hour following operation the blood pressure had risen to 100/60 and the pulse rate had fallen to 100. The blood pressure promptly returned to normal. A third case in this group illustrated in a striking way the excellent tolerance of patients for this approach. The patient was a 72 year old man with carcinoma involving the esophagogastric junction. While on the ward, the patient's lesion began to bleed suddenly and with continued hemorrhage over a period of several hours, his blood pressure fell to 70/40 with typical signs of profound shock. He was in shock when the anesthesia was started. His blood pressure rose during the transthoracic gastric resection which included a splenectomy and partial pancreatectomy. At the end of the procedure the patient's blood pressure had risen to 110/84 with a pulse rate of 108, his skin was warm and dry and his color good. Rapid recovery from shock took place notwithstanding the anesthesia and transpleural operation and also despite a 1½ hour period of difficulty in getting a transfusion started during the operation.

Briefly, then, 1 patient in the transabdominal wall group (ether) developed shock as a result of the anesthesia and operation. In the transpleural group no patients developed shock although there were 2 instances of low blood pressure after long procedures. Another patient in whom shock had developed *before* anesthesia and operation were started recovered from shock during the transthoracic procedure. As far as these data go, both procedures are well tolerated.

The data Table I cannot be considered in any precise mathematical way: they are too few; they do afford, however, a useful sample of a larger body of information of which they are typical. Thus during transpleural surgery under ether, the relative constancy of the systolic blood pressure, the constancy of the diastolic pressure and the pulse rate are evidence that what we might call the patients' circulatory equilibrium is being maintained to a remarkable degree. Since this is so despite prolonged, increasingly adverse conditions (surgical trauma, blood loss, heat loss) this state must be maintained by active, finely balanced compensatory mechanisms. We can generalize from the constancy of the systolic and diastolic pressures and the unchanged pulse rate that the effective cardiac output probably continues unchanged even throughout 4 hours. During these 4 hours we know that the patient is subjected to prolonged deleterious stimuli; notwithstanding these evident facts his diastolic pressure persists

TABLE II.—FIFTY RECENT GASTRIC RESECTIONS FOR CARCINOMA

10 Patients in Each Group

Anesthesia	Duration	Patients			At entry	Time following induction							
		Sex		Av. age		1 hr.		2 hrs.		3 hrs.		4 hrs.	
		M.	F.		Blood pressure	Blood pressure	Pulse	Blood pressure	Pulse	Blood pressure	Pulse	Blood pressure	Pulse
Ether Transpleural operation	3 hrs. 59 min.	8	2	55.8	119/70	110/73	99	116/78	105	112/77	103	[1]107/73	102
Ether Transabdominal wall operation	2 hrs. 54 min.	8	2	54.2	131/83	132/76	106	133/80	106	116/72	109		
Spinal Transabdominal wall operation	2 hrs. 16 min.	7	3	57.7	137/81	109/68	92	109/69	102				
Splanchnic Block Transabdominal wall operation	2 hrs. 37 min.	6	4	61.1	136/78	111/65	96	125/72	98				
Local Transabdominal wall operation	2 hrs. 13 min.	7	3	63.2	127/80	104/65	93	106/68	88				

unchanged. Apparently it can only have been maintained unchanged by active processes compensating for the obvious opposing factors (anesthesia, surgical trauma, blood loss). At the end of operation these patients customarily are warm. The skin of the forehead shows a very active capillary circulation as indicated by immediate reflushing of areas blanched by light pressure.[1] The pulse is full and of good quality.

When the resection of the stomach is carried out through the abdominal wall under ether anesthesia, the systolic and diastolic pressures and the pulse rate persist unchanged as presumably the cardiac output does also; active peripheral constriction must have been occurring to oppose the influence of the obvious blood loss and the other deleterious factors, yet after 3 hours of anesthesia and gastric surgery through the abdominal wall in this rather old group with cancer, the typical patient is pale, cool, and sweating, with a pulse of rather poor quality.

Although no significant differences in the systolic or diastolic pressures or the pulse rates of these two groups were observed, it is evident that after 4 hours of gastric surgery through the thorax the general appearance of the patients in this group is better than it is after an even shorter intervention through the abdominal wall. On the basis of the data at hand and the experience to date it appears to be safe to say that gastric surgery through the thorax is no more shock-producing and perhaps even less so than *gastric surgery carried out through the abdominal wall.* There are reasons why this should be so. The clearer cut ones can be summarized briefly:

a. *Gastric surgery through the thorax can be carried out at a far lighter level of anesthesia* than is possible when the anterior abdominal wall route is used. In the former case relaxation of the abdominal wall is not necessary. The only relaxation needed is that of the diaphragm, and this can be obtained by a drop or two of procaine injected into the phrenic nerve under direct vision.

b. When the transabdominal wall route is used, the surgeon is constantly disturbing the large blood vessels and nerve plexuses of the abdominal cavity; he constantly subjects the pedicles of the abdominal organs to pressure or to tension. *These actions are well known to produce harmful circulatory effects,* and ultimately a fall in blood pressure. There is relatively little disturbance of the intra-abdominal structures adjacent to the stomach in the transpleural approach.

It will also be a matter of great interest to observe, when adequate data have accumulated, if gastric surgery carried out with light anesthesia and without an abdominal incision is followed by a lower incidence of postoperative pulmonary complications than is true following the abdominal incision. There are good reasons for believing that such may prove to be the case.

The evidence suggests that in the hands of a properly qualified operating team, when the gastric lesion is such that it can for anatomical reasons be more easily approached through the transdiaphragmatic route, there is no reason to fear more "shock" with this approach than with the

[1]This is a very useful test for following the decrease in skin circulation which precedes the onset of shock. Normally, reflushing of the skin occurs in a second or less after blanching by light finger pressure. With slowing down of the peripheral circulation an appreciable delay is easily apparent.

traditional transabdominal wall approach. Certainly this is only one aspect of the problem and other possible hazards beyond the scope of this study must be evaluated before the transpleural approach can become standard procedure.

Further data of value are apparent in a comparison of the blood pressure responses under ether and spinal anesthesia, in the group undergoing gastric resection for cancer (Table II). Under spinal anesthesia, unlike the circumstances when ether is used, even at the end of the first hour, the circulation shows definite impairment: the peripheral resistance has been unable to compensate adequately; the cardiac output is unable to correct for this—not seriously so, but appreciably. It should be emphasized that this trend is not easily apparent from the examination of individual records. There is much more fluctuation of blood pressure and pulse rate during the course of operation in the course of a few minutes under spinal than is true under general anesthesia. This finding only becomes apparent when a considerable number of records are studied consecutively at one time. This fluctuation undoubtedly indicates strain on the circulatory system.

The changes encountered here in these average data are deceptively small; they show trends, not what may happen in an individual case. All of this information might be put down as so much academic straining over inconsequentials if it did not lead to the increasingly widely recognized observation that patients acutely subjected to trauma and to blood loss do in fact withstand spinal anesthesia less well than they do general anesthesia. The majority of reports from the European battlefields of this war as well as many reports from the previous war concur in this. Unhappily it is also roundly borne out by information now coming in from our own battle zones. *Spinal anesthesia is a poor procedure to use in the seriously wounded, or in the seriously impaired individual in civil practice.*

In the group operated upon under local-splanchnic block anesthesia the circulatory results at the end of the first hour are comparable to spinal, as might be expected. Interestingly enough, when sufficient time has elapsed for the splanchnic block to have waned, the blood pressure shows an upward trend. (Splanchnic block was frequently supplemented by light evipal soluble or pentothal sodium or ether anesthesia.)

The patients operated upon under local anesthesia were obviously older, poorer risk patients. It is not fair to compare these data with the other groups. The inability of the circulatory system of the impaired individuals of this last group to maintain original levels is plain; it was to be expected that this would be the case.

THE TECHNIQUE OF ANESTHESIA FOR TRANSPLEURAL GASTRIC SURGERY

At the present time the anesthetist for thoracic surgery needs no more equipment than he does for a well conducted cholecystectomy. With one or two notable exceptions, the evolution from which present practices have grown has consisted not in acquiring new appurtenances but in discarding old ones. At the present time our technique has been reduced to what seems to require a bare minimum of equipment. Consideration of this may make the technique of anesthesia for transpleural surgery appear simple, and it is simple, although consideration of equipment alone may make it appear deceptively so. I wish neither to exaggerate its complexity nor to underrate it. A primary aim of the work here has been to determine the essentials of a satisfactory technique, to show that a simple technique carried out with the equipment found in or easily obtainable by all reasonably well equipped hospitals, equipment familiar to well trained anesthetists, is adequate for this group of cases, provided certain practices are unfailingly observed.

In the transpleural approach to the upper abdominal viscera, the anesthetist can make a considerable contribution, for the anesthetist experienced in providing anesthesia for thoracic surgery can make it possible for the well trained general surgeon to operate in this field. The man who is experienced in gastric surgery can still do the gastric surgery, by whatever route a given lesion indicates the choice to be. He is limited in the main by the experience and training of his anesthetist.

Reference has been made to the essentials of an anesthesia technique for transpleural surgery. Elsewhere the principles (1) of anesthesia for this group of cases have been considered as well as the arguments (2) for and against certain current practices in this field. I shall not repeat these in detail here. From anesthesia for several hundred major procedures through the open pleura we have concluded that the anesthesia for this group of cases should include, if the mortality is to be kept low, the following:

Ether anesthesia briefly induced with nitrous oxide is our choice. This is occasionally supplemented with procaine block of the vagus nerve and its pulmonary plexus as well as by frequent block of the phrenic nerve. Ether greatly depresses the activity of the vagus, a desirable condition

which we occasionally augment by rather large doses of atropine. Under ether, sensitivity of the respiratory center to carbon dioxide is preserved, a characteristic of great importance. The carbon dioxide blood level does not rise under ether as it does under certain anesthetic agents (4). Barbiturates, for example, in general anesthesia lessen and finally destroy the sensitivity of the respiratory center to carbon dioxide with sometimes fatal results, experimentally at least, but under circumstances very like those encountered in many clinical deaths.

Intratracheal intubation is essential, for it is only with an intratracheal tube in place that an open airway can be assured at all times. In our opinion it is unecessary and unwise to use an inflatable cuff on these tubes. An intratracheal tube once in place eliminates the necessity for more or less frequent manipulation of the patient's head and jaws in an effort to improve the airway. Meddling here necessitates a deeper level of anesthesia than is the case if an intratracheal tube is in place and the airway left undisturbed. Reflexes from such a foreign body in the airway quickly fatigue and disappear. Thus, during wound closure the patient whose respiratory exchange will be excellent through the tube can be allowed to get very light, so that he has nearly recovered from the influence of the anesthetic at the end of the operation. The presence of the intratracheal tube also makes it possible to combat another possible hazard of the transpleural approach: the sudden, acute pulmonary edema which may develop if one lung long remains collapsed. If the transpleural approach to the stomach is to be of wide usefulness in the surgery of malignant disease, it should be possible to employ it in the aged. Elderly patients in this group may be prone to develop gross pulmonary edema if one lung is allowed to remain acutely collapsed. In no patient should the lung be allowed to remain collapsed for more than 30 minutes or so at a time. Only further experience with the aged group can tell us how often this accident will occur. In the meantime, facilities should be at hand to cope with it. An intratracheal tube is an indispensable aid in handling such a situation. Facilities for rapid bronchial aspiration, as well as positive pressure anesthesia when necessary, are important. A closed gas machine with carbon dioxide absorption and a tight face mask complete the list of essentials.

All parts of the technique referred to are essential if the major hazards of this type of anesthesia are to be overcome; namely, low blood oxygen, high blood carbon dioxide, obstructing secretions, troublesome reflexes, including cough. Adequate provision for combatting these hazards must be made, we believe, if the transpleural approach is to be used successfully in gastric surgery.

The proper conduct of these cases requires that the rôle of the anesthetist be broadened. The anesthetist must take the responsibility for protecting the patient from needless strain. He warns against unnecessary heat loss in a too cold operating room; he minimizes harmful vagal reflexes by requesting that the vagus nerve or its branches be blocked with local anesthesia when cardiac and respiratory variations indicate the need, or he diminishes vagal activity by administering atropine; he watches for prodromal signs of shock and when necessary warns the surgeon of their development; he directs the administration of blood or blood substitutes; he guards against oxygen shortage or carbon dioxide excess.

CIVIL EXPERIENCE APPLICABLE TO ANESTHESIA FOR THE SURGICAL TREATMENT OF MAJOR WAR INJURIES OF THE THORAX

In the decade just passed it has been possible to distinguish between the dispensable and the indispensable anesthesia practices common in thoracic surgery. Great simplification has been possible in these. The excellence of ether anesthesia and the irreducible minimum of equipment necessary has been emphasized in this article and in the papers referred to in the discussion of the principles and procedures concerned.

The importance of the demonstration that simple procedures in this field are at least as effective as the many more complicated ones so often recommended becomes evident when it is recalled that an examination of battlefield dead of the last World War has shown that one-third died of chest injuries. Unquestionably many of these could have been saved by proper treatment. In the past the number of military deaths due to chest injuries has depended in large part upon the delay and distance to be overcome before these wounded can be transported to a hospital for definitive treatment.

We know that in the field of thoracic surgery more than in any other surgical field prompt treatment must be brought to the wounded patient rather than the other way around, if the patient is to be saved. The increased effectiveness and simplification of modern supportive measures and the simplification of anesthesia procedures go far to make thoracic surgery possible in combat zones. It is also apparent now that if the chest be open many abdominal procedures can be carried out through this same incision without unduly jeop-

ardizing the patient. This fact may be of use in military surgery.

The simplification of anesthesia principles and procedures important in thoracic surgery makes possible the rapid training to the point of adequacy of those who have had no special anesthesia experience in this field. *It is easier to train an anesthetist to the degree where he can make it possible for a well trained general surgeon to cope adequately with battlefield problems of thoracic surgery than it is to train a specialist in thoracic surgery.* However able the specialist may be he will be sadly handicapped if he must contend with poor anesthesia. However able the anesthetist may be he will seriously handicap his entire team if he insists upon elaborate equipment or procedures (3), already shown to be unnecessary in civil practice and certainly unnecessary in mobile, battlefield surgery.

The anesthetist who is familiar with the problems of anesthesia for thoracic surgery can make it possible for the thoracic surgeon to proceed with deliberation in exploring thoracic wounds of warfare. It is the anesthetist who makes it possible for the surgeon to exercise the deliberation necessary for the proper control of hemorrhage, proper débridement of the wound, and to determine carefully what shall be done at once and what postponed. It is the anesthetist who makes it possible for the surgeon with only a general surgical training to work with success in this field.

SUMMARY

1. In a series of gastric resections for carcinoma, the tolerance of patients for the traditional transabdominal wall approach under ether is compared with their tolerance for the transpleural approach under ether, as far as surgical "fatigue" is concerned. It is observed that those in the transpleural group tolerate the operative procedure at least as well and perhaps better than those in the other group. Thus when the transpleural route is indicated for anatomical reasons and when the operating team is experienced, it appears that the poor risk patient does not necessarily rule out the high approach.

Reasons for the patients' excellent tolerance for the transpleural approach to the stomach are found in the fact that in transpleural gastric surgery a far lighter level of anesthesia is possible than is true in the case of the transabdominal wall approach. In the former case the only relaxation needed is that of the diaphragm, obtained by block of the phrenic nerve under direct vision. Furthermore, in the transpleural approach to the stomach disturbance of the other abdominal viscera, well known to cause harmful circulatory effects, can largely be avoided.

2. When the gastric surgery is carried out through the anterior abdominal wall, evidence is presented that the circulatory system tolerates ether anesthesia better than spinal or splanchnic block anesthesia.

3. The indispensable anesthesia procedures used in performing transpleural gastric surgery are considered.

4. Lessons learned in civil practice that are applicable to anesthesia for surgical treatment of war injuries are considered.

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A MODIFICATION OF THE CALLANDER AMPUTATION

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THE Callander amputation has received wide recognition since its description (1935), and justly so, for it possesses certain definite advantages. As its originator has so strongly emphasized, the section goes through muscle tendons instead of muscle bellies, thus reducing the operative trauma and shock. Since the operative procedure is confined to the popliteal fossa, the spread of infection proximally along muscle planes is interfered with. The omission of deep sutures lessens the possibility of infection and favors primary union. The outline of the skin incisions, as shown by Callander, corresponds roughly to the distal extension of the collateral circulation when block is present in the popliteal artery. The absence of drainage material, though a detail, is also important in the avoidance of secondary infection and delayed healing.

It is not within the scope of this paper to discuss the proper level of amputation, upper, middle, or lower thigh, knee (Callander), or proximal part of leg, under various pathological conditions. Suffice it to say that this depends, in my opinion, upon the type of pathological lesion—trauma, peripheral vascular disease, infection—and the condition of the circulation—main and collateral—in each individual case (see Grodinsky, 1938). However, since most leg amputations are done because of peripheral vascular disease, such as diabetes, senile arteriosclerosis, Buerger's disease, they are usually done high, at or above the knee, to insure healing of the stump.

Amputations through the middle or proximal thigh are accompanied by considerable postoperative shock due to cutting through muscle bellies and sometimes result in poor stumps for the use of artificial legs. The Gritti-Stokes operation was an earlier attempt to get high enough for good healing and still have a good stump for weight bearing. Its great fault lay in the uncertain and insecure union of the retained portion of the patella to the cut end of the femur. The Callander operation, by removing the patella and transecting the femur just above the articular surface, has obviated these difficulties while retaining the other advantages of the Gritti-Stokes procedure.

However, the Callander operation has, in my opinion, one serious fault, that of long skin flaps. It has long been recognized that short flaps, or no flaps at all, favor primary union in amputations for peripheral vascular disease. It is true that the collateral circulation, in case of occlusion of the popliteal artery in the popliteal fossa, is usually sufficient to maintain vitality in the skin and subcutaneous structures roughly corresponding to the proximal third of the leg. However, this is only true under conditions of rest and protection. When the trauma of operation, no matter how gently performed, is added to the picture, the outcome is often different. It has been my misfortune and that of others (e.g. Pearl, 1941) to have had several cases of sloughing or slowly healing flaps following the classical Callander operation. For that reason, I gradually modified the operation by progressively shortening the flaps, while retaining the other essential features of the original operation. The results by the technique thus gradually evolved have been, in my experience, far superior to those with the original operation as regards healing time and satisfactory stumps. The modified technique of Pearl (1941) is, in my opinion, inadequate because the skin flaps are still too long, the patellar bed is not retained to support the lower end of the femur, and the latter is transected higher than necessary.

TECHNIQUE

Incisions. No tourniquet is used in any amputation done because of peripheral vascular disease for fear of further damaging diseased blood vessels. The skin preparation and draping are done in the usual manner. With the operator standing to the medial side of the leg to be amputated and with the knee slightly flexed, the skin incision (Fig. 1) for the anterior flap is started just distal to the patella and carried medially in a curved direction to a point about 1 inch proximal to the medial condyle of the femur. Then it is carried laterally in a similar manner to a point about 1 inch proximal to the lateral condyle of the femur. The posterior flap is made the same length as the anterior one, and the incision, starting in the popliteal fossa opposite the distal border of the patella, extends in both directions to meet the medial and lateral ends of the anterior incision already made. This is practically a circular incision with slight proximal extensions medially and laterally to facilitate the exposure and section of the deeper

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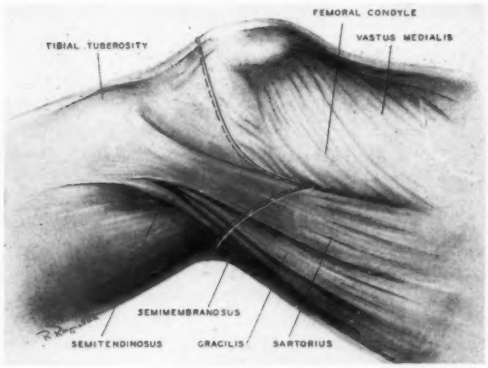

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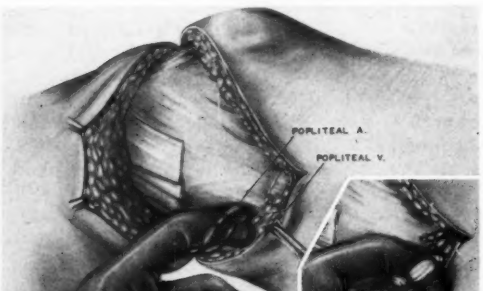

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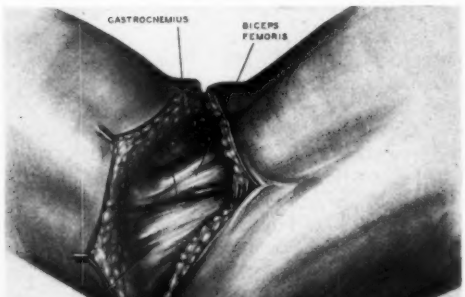

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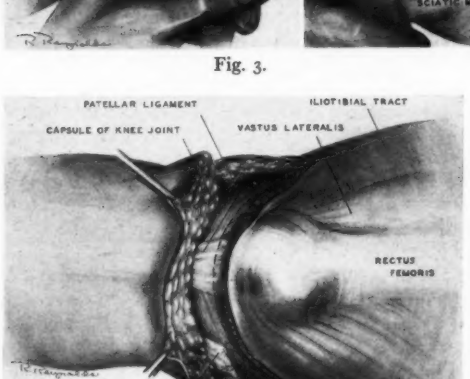

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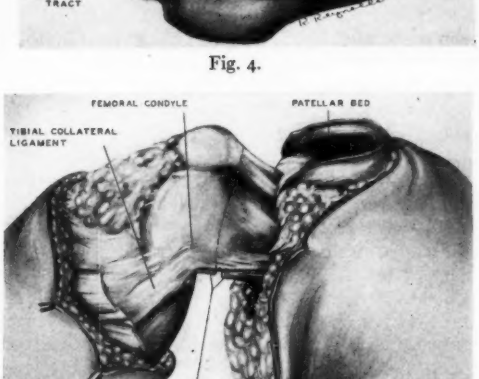

Fig. 6.

Fig. 1. Medial aspect of right knee region, showing outline of skin incisions—medial in solid lines and lateral in broken lines—in relation to bony prominences and muscles. Note short, equal flaps.

Fig. 2. Deep view, medial side—tendons of medial muscles being elevated for section in line with skin incision.

Fig. 3. Deeper dissection from medial side, showing method of delivering and doubly ligating popliteal vessels.

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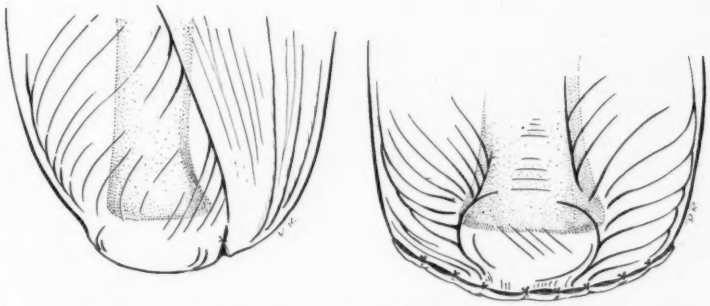

Fig. 7. Diagrammatic transparency drawings of stump, medial and anterior views, showing relation of the end of the femur to the overlying muscles and to the suture line. Note how the patellar fossa fits over the lower end of the femur.

structures. The medial extension should pass between the vastus medialis and sartorius muscles and the lateral extension between the iliotibial tract (the continuation of the tensor fascia lata) and biceps femoris muscle.

Treatment of medial side and popliteal fossa. With the leg rotated laterally, the skin incisions are deepened both anteriorly and posteriorly from their middle to their medial extremities, so as to expose the tendons of insertion of the sartorius, gracilis, semitendinosis, and semimembranosis muscles. Each of these is transected opposite the proximal border of the skin, the skin having retracted somewhat by this time (Fig. 2). This exposes the popliteal space containing the main vessels and nerves. The popliteal artery and veins are easily delivered into view, doubly ligated with No. 2 chromic catgut and severed between ligatures (Fig. 3). An additional ligature on the proximal side of the artery is usually desirable. The tibial and peroneal nerves are likewise delivered from the fossa, either together or separately, depending on the individual case. They are also doubly ligated with plain or chromic catgut, injected between the ligatures with 1 to 2 cubic centimeters of 95 per cent alcohol, and then transected through this area, between the ligatures. As pointed out by Pearl (1941), this method of alcohol injection prevents proximal extension of the alcohol and undesired effects therefrom.

Treatment of lateral side. By rotating the limb toward the operator, a good exposure of the lateral aspect may be obtained. The lateral halves of the anterior and posterior incisions are deepened to expose the iliotibial tract and the tendon of the biceps femoris muscle. These are transected opposite the proximal border of the skin incision in the same manner as the tendons of the medial side. The remaining soft—areolar—tissues in the popliteal fossa are likewise transected opposite the proximal border of the skin incision, thus completely freeing the posterior as well as the medial and lateral surfaces of the femur (Fig. 4).

Anterior dissection. With the limb in the original position, the anterior incision just distal to the patella is deepened so as to extend through the patellar tendon and its medial and lateral extensions and expose the knee joint (Fig. 5). The patella is quickly cut from its bed without attempting to destroy the adjacent serous surface.

Transection of femur and treatment of stump. The insertion of the adductor magnus is separated from the adductor tubercle and, after the soft tissues are protected by towels, the operator transects the femur just proximal to the adductor tubercle with ordinary or Gigli saw (Fig. 6). The edges of the bone are smoothed off with a file or rasp and the bleeding points sealed with bone wax. The soft tissues of the stump are irrigated with warm saline solution to wash out all débris and bone dust, and the bleeding points are ligated with fine plain catgut. No deep sutures are placed but the skin flaps are loosely brought together by

preliminary to sectioning between ligatures. Note additional ligature on proximal side of popliteal artery. Insert shows method of delivering and doubly ligating sciatic nerve, before injecting with alcohol and sectioning between ligatures.

Fig. 4. Lateral view of rotated right knee region, showing deepened skin incision with exposure of the iliotibial tract and the biceps femoris muscle. The site of section of the tendon of the latter, on level with the skin incision, is indicated by the broken line.

Fig. 5. Anterior view of right knee region, showing deepened skin incision, and site of section through patellar ligament and capsule of knee joint, broken line.

Fig. 6. Deepest view of anteromedial aspect, showing sectioned muscle tendons, vessels and nerve, the patellar bed after removal of the patella, and the line of section of the femur, just above the adductor tubercle.

widely spaced skin clips or dermal sutures, leaving sufficient spaces between clips or sutures for drainage (Fig. 7). Usually, only three or four clips or sutures are needed on each side. After 48 to 72 hours, when most drainage has ceased, additional clips or sutures may be placed between the original ones for better coaptation. Ordinary dry dressings are applied, a good dressing being a 5 yard roll followed by a flannel or gauze bandage. Ordinarily, traction is unnecessary and the patient is returned to bed with the stump slightly flexed on pillows.

After treatment. In the absence of excessive fever or pain, it is not necessary, in fact undesirable, to redress the wound before 72 hours have elapsed. At that time, if the drainage has apparently ceased, the additional clips or sutures may be introduced and the stump dressed as before. In the absence of further temperature reaction or other untoward symptoms, the stump does not have to be examined again until the 8th day when alternate clips or sutures are removed. The remaining clips or sutures are removed between the 10th and 14th days, at which time, if healing is by primary or almost primary union, the patient may be dismissed from the hospital and treated thereafter at home or in the out patient department.

RESULTS

Although the flaps are not as long as in the original Callander operation, they are of sufficient length to permit easy closure of the skin as described. As usual, the greater retraction of the hamstrings brings the scar posteriorly, so that even with an end bearing artificial limb, a painless scar results. As in the Callander operation, the patellar bed covers the end of the femur forming a satisfactory pad for the latter. A smooth conical stump results which facilitates the fitting of an artificial limb if one is to be worn.

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THE SHOCK CART

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IN THE study of surgical shock cases at the Presbyterian Hospital, New York, we have found that by assembling equipment on a cart the time for obtaining objective data has been shortened by taking the laboratory to the patient's bedside.

For the past 5 years, certain simple tests have given us a clearer and less subjective approach to the question of what to do in acute emergencies; what fluids to select and above all when fluid therapy should be changed or stopped (4).

These tests supplement a careful history and physical examination. They are:

1. *Specific gravity* of *peripheral blood* (1, 2). It is here that changes first appear. Hemoconcentration in the *capillaries* foretells of the approaching fall in blood pressure.

2. *Hematocrit* on *venous blood.* In shock, excluding that due to hemorrhage, a decreasing hematocrit indicates that blood volume is being restored. On the other hand, should repeated hematocrits or repeated determinations of specific gravity of capillary blood reveal that hemoconcentration is occurring in spite of therapy the warning is clear; either, the lesion is overwhelming, or, the supportive therapy is insufficient or wrong and should be changed.

3. The *specific gravity* of *plasma.* This is done on the supernatant fluid in the hematocrit tube.

4. *Total plasma protein.* From tables, the specific gravity of the plasma is readily translated into total protein concentration according to the formulas of Weech, Reeves, and Goettsch, or Moore and Van Slyke.

Every hematocrit should be checked by total protein determinations. We recommend that a base line be secured on admission, or as early as feasible, and that repeated determinations be instituted. Single values are of little importance. Trends in hemoconcentration or hemodilution are significant.

Elapsed time for tests. With a little practice, the specific gravity of plasma or capillary blood can be ascertained within 2 or 3 minutes. We usually spin the hematocrit for 1 hour to secure ultimate packing. In emergencies, the centrifuge can be stopped at the end of 15 minutes. This reading will be within 5 to 10 per cent of the true value.

In addition to diagnostic procedures, therapeutic remedies such as liquid or dried plasma, isotonic or hypertonic (5%) saline, whole blood, and adrenal cortical extract can be easily transported on this cart. If there are a number of casualties, the cart affords space for carrying sufficient blood and other remedial measures.

Field transportation. A carrying case for the falling drop apparatus, hematocrit tubes, solutions, etc., has been used in trips about the country and in journeys abroad. This case has been tested out in all kinds of travel from the airplane

Fig. 1. The shock cart. The following items are carried on the cart: alcohol; tourniquet; sponge jar; sponge forceps; sterile sponges; lancet; kidney basin; hematocrit tubes with heparin; test tube rack for hematocrit tubes; sterile, dry 20 c.c. syringes; ammonia, water, alcohol and ether for cleaning pipettes; falling drop apparatus; pipettes; pipette holder; stopwatch and stand; alignment chart; specific gravity standard solutions; extra xylene-bromobenzene mixtures; centrifuge; pencil; paper; flashlight. Cut down set for cannulation of veins.

From the Surgical Pathology Laboratory of the College of Physicians and Surgeons, Columbia University, and the Department of Surgery, the Presbyterian Hospital, New York, New York.

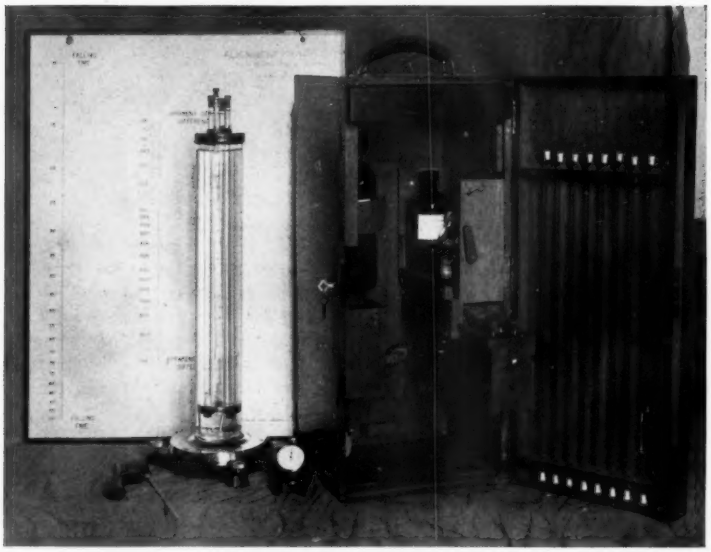

Fig. 2. Carrying case.

to an ox cart. The use of a hand centrifuge obviates the necessity for electrical power.

Distribution of apparatus. In 493 hospitals and laboratories these tests have been adopted.

Finally, in the training of young surgeons for the armed forces, it should be the duty of those who remain behind in the teaching centers to instill the necessity of the present quantitative approach to shock and to have these students follow such cases with these exact measures.

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AN AMBULATORY METHOD OF TREATMENT FOR INTERTROCHANTERIC FRACTURES OF THE FEMUR

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ONE of the most frequent accidents of later life is fracture of the hip. Until the development by Smith-Petersen of the three flanged nail, at a time when isoelectric metals were available, no outstanding advance had been made in their treatment. While this nail was successful in the treatment of intercapsular fractures it did not solve the problem of fractures in the intertrochanteric area, especially when severe comminution was present.

The following is a description of a method of fixation that is applicable in any type of intertrochanteric fracture. It does not confine the patient nor require an incision; it immobilizes no joints and permits early crutch ambulation. No other method described in the literature combines its simplicity, universal application, or its advantages. Fifty-four patients have been treated by this method, 22 of which by other operators.

There is wide variation in the position of the fracture lines and in the degree of impaction and comminution in intertrochanteric fractures of the femur. The fracturing force and muscle spasm tend to pull both fragments upward, creating a coxa vara. The lower fragment, if not impacted, tends to fall backward and into external rotation, due to the weight of the extremity. The lesser trochanter may be detached, especially in severe comminution, or may remain intact with the proximal fragment, in which case the proximal fragment tends to be displaced upward along the course of the iliopsoas.

Regardless of the method of treatment, accurate reduction and firm fixation of the fragments are necessary in order to obtain early union. Reduction is usually made possible through longitudinal and lateral traction, while the distal fragment is lifted, abducted, and internally rotated. The usual attempts at immobilization are made through the medium of a body cast, with or without traction; or such forms of traction as are used with the Thomas or Hodgen splints; or traction on the principle of the Roger Anderson well leg method. Open operation with fixation by means of a combination of plates, nails, or screws may be used in the less comminuted types.

The use of a body cast, or any method of traction, requires a long period of close confinement. It may be necessary to maintain the abduction and traction treatment for a period of 6 months or more to secure solid union, because if fixation is not complete, union may be delayed. If the limb is freed before union is firm, muscle pull acting on the soft callus results in a coxa vara and infrequently in nonunion. The use of a plate with a nail or screw is not a simple procedure. The equipment is expensive and its use is of limited application because it is not suitable for many severely comminuted fractures.

In treatment by means of a body cast or a method of traction, nursing care is often a serious problem because of the distress of confinement, discomfort of incomplete fixation, pain of pressure sores, hypostatic pneumonia, or because of the physical and mental deterioration that follows long immobilization in elderly people. Even after the fracture has healed invalidism may persist due to stiff knees and hips or to the physical weakness that follows long inactivity.

In this method fixation of the fragments is secured through the closed insertion of four pins. Two pass within the neck into the head of the femur and are firmly united with two passing at a converging angle through the upper end of the distal fragment. This unit creates a solid bridge across the fractured area between the head and the upper end of the distal fragment of the femur and accomplishes complete fixation in any type of intertrochanteric fracture. The patient is not confined, may move about in bed immediately following the operation, and be up in a chair, the more active patient be on crutches, in a few days. All joints are kept mobile, so that the patient's strength is better maintained and his mental attitude kept more cheerful. As a result, pressure sores, pneumonia, and degenerative changes are less frequent, which fact greatly simplifies nursing care, shortens hospitalization and duration of disability following healing.

In the care of an intertrochanteric fracture, treatment of shock is undertaken immediately. This treatment will usually include traction immobilization of the extremity. Early reduction and fixation of the fragments are desirable, for they will minimize shock and lessen the incidence of physical and mental exhaustion.

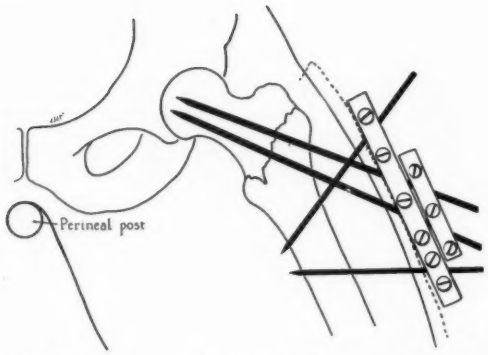

Fig. 1. Anteroposterior view of the fixation in place. The dotted line represents the initial plaster first applied. The long clamp is on the two distal pins, and the short one on the two proximal ones. This unit is later incorporated in a plaster cast to the thigh as described.

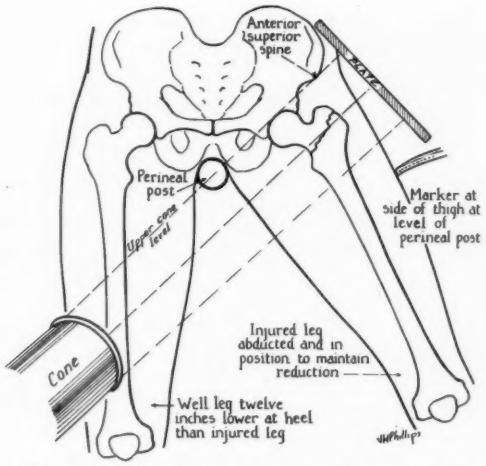
Anterior superior spine
Perineal post
Upper cone level
Marker at side of thigh at level of perineal post
Injured leg abducted and in position to maintain reduction
Cone
Well leg twelve inches lower at heel than injured leg

Fig. 2. View from above when lateral x-ray films are taken. The marker shown is used as a guide for the insertion of the first pin when the anteroposterior view is taken.

For reduction, the anesthetic needed will vary with the patient. The routine use of 1½ grains of nembutal with 1/6 grain of morphine and 1/200 grain of scopolamine an hour before surgery will suffice for reduction in a number of patients, while the addition of 20 to 30 cubic centimeters of 1 per cent novocain injected into the fracture site will permit reduction in the majority. However, the most satisfactory state of anesthesia is obtained by the additional use of pentothal, very little being required for narcosis.

After reduction the legs are immobilized in traction, with the injured member parallel to the floor, abducted, rotated, and with traction sufficient to maintain the reduction. The uninjured leg is extended but permitted to drop about 12 inches lower at the heel than its fellow in order to facilitate the taking of lateral roentgenograms. Anteroposterior and lateral x-ray films are always taken to check the reduction and placement of pins. Unless they are properly taken the results may be most misleading and time consuming. The ray must be centered on the neck in both the vertical and horizontal planes, and repeat x-ray films must be taken from the same viewpoint. If not properly centered distortion may cause a poorly placed pin to appear well placed, while films taken from various viewpoints have little value for comparison. The center of the proximal portion of the head will lie at a point approximately ½ inch below the midpoint of a line joining the anterosuperior spine and the lower border of the pubis. A perpendicular line intersecting this point will approximate the center of the neck, and to obtain the anteroposterior view the ray should be centered 2 inches distally along this line. The lateral view is obtained by placing the tube at the side of the well leg with the cone directed over the leg. The rays should be parallel to and include the line joining the anterosuperior spine and the peroneal post, the plate being held well in the flank at right angles to the cone. This technique will permit repeat x-ray films from the same viewpoints, the alignments being easily and quickly made without movement of either extremity. As most of the older fracture tables, such as the Hawley, have an iron pelvic rest and peroneal post, it is necessary to replace them with wooden units in order to use this technique; otherwise the head will be undefined in either view, being obscured by the metal parts.

Reduction being satisfactory careful surgical preparation is made of the thigh before insertion of the pins. First to be inserted are those which are to pass through the neck into the head of the femur to control the proximal fragment. These pins are 6 inches or more in length, depending upon the depth of the soft tissues, 5/32 inch in diameter, sufficiently heavy to support the weight of the patient in case of weight bearing, and are easily inserted by means of a T handle. The correct placement of the first of these upon the initial attempt is the most difficult part of the procedure. As a guide for the selection of the point of insertion, a marker is placed on the lateral surface of the thigh at the level of the peroneal post when the anteroposterior view is being taken. This film will indicate a point in relation to the marker at which the pin must enter the soft tissues in

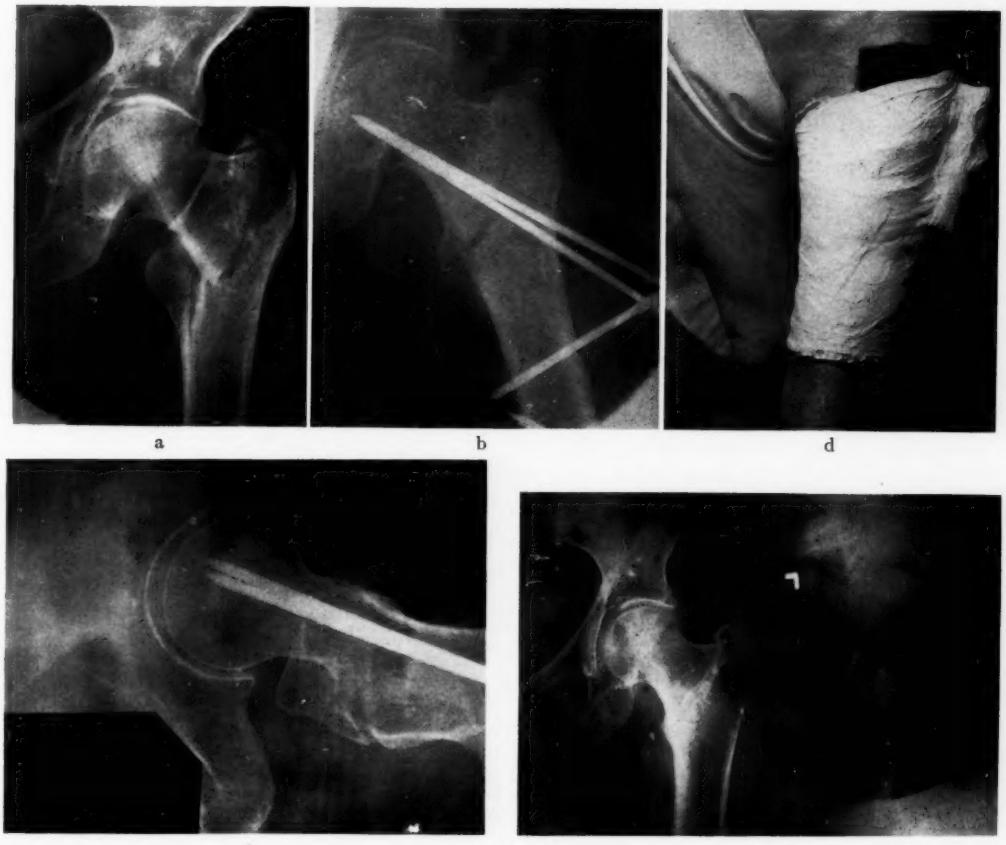

Fig. 3. Case 2. a, February 18, 1941, fracture in an 84 year old female. b, February 20, 1941, anteroposterior view of reduction and fixation pins in place. c, February 20, 1941, lateral view of reduction and pins in proximal fragment. d, March 12, 1941, view of fixation. Patient had been on crutches 1 week. e, October 27, 1941, final result. Excellent functional result. The pins were removed May 6, 1941.

order to enter and parallel the long axis of the neck of the femur in the horizontal body plane. The lateral view will indicate the amount of inclination needed to parallel the long axis of the neck in the vertical plane. After the point and angles of insertion have been determined, the pin is felt to pass easily through the soft tissues and strike the relatively dense cortical surface. When it is through the cortex, it passes readily through the neck and strikes the compact bone of the head into which it should enter about 1 inch. X-ray films are then taken to check the position and the second pin is inserted, with the position of the first used as a guide. If the first was not properly placed it may now be adjusted.

Control of the distal fragment is secured by two additional pins in its proximal end. These are 5 inches or more in length and are $^{4}/_{32}$ inch in diameter. They are inserted at an angle to one another so that they bear the same relation as two sides of a triangle to one another. Each must pass through both cortical surfaces of the femur and preferably in the same horizontal body plane as those in the proximal fragment. These two pins utilize the principle of the Roger Anderson half pin unit, a number of which were used in this series to secure the distal fragment.

Sterile dry dressings are placed over the pins, and a layer of sheet wadding is applied about the thigh, followed by a number of turns of plaster

which embrace the pins and firmly and smoothly press the soft tissues along the pins toward the shaft. To secure complete fixation of the fragments the four pins must be firmly united with one another, and to unite them more firmly than is possible with plaster alone two flat pieces of metal bar in the shape of tongue blades, which have been drilled and tapped so that they may be tightened together by means of a number of screws or bolts, are used as a clamp over the pins. A clamp is placed about each set of pins, made snug against the plaster that has been applied, and solidly tightened on the pins. The clamps and pins are united by plaster and incorporated in a light cast to the thigh, its extent being such that free motion of the hip and knee is possible.

Immediately after the cast has hardened the thigh and knee should be put through a full range of motion. This will separate the fascia and muscles along the pin tracts and lessen the discomfort of early active motion. The day following the operation the patient may sit up in bed and, as his general condition improves, be up in a wheelchair and on crutches. In the meantime immediate passive motion is made gently daily in the hip and knee and active motion insistently encouraged.

The pins are left in until union is solid, as disclosed by x-ray film, which is usually within 6 to 10 weeks.

In the application of this method certain factors will contribute to its success and to the comfort of the patient. Special effort should be made to insert the pins so that the soft structures are without tension, for when tension is present there will be discomfort and pressure necrosis with exudate. The presence of exudate or bleeding about the pins will result in moist dressings and is an invitation to infection. Early active motion must be insistently developed and this is facilitated through early gentle passive motion and use of the wheelchair with the leg in flexion.

The only points of solid fixation of the pins in the proximal fragment are those portions which are in the head. For this reason they should be inserted well into the head and below the upper margin, especially in case of long standing trophic disturbance, because the constant muscle pull and occasional weight bearing may cause them to cut through the softened head and neck and result in loss of fixation.

In conclusion a method of multiple pin fixation is presented for all types of intertrochanteric fractures of the femur. It is simple in application, requires no incision, immobilizes no joints, and permits early crutch ambulation.

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ARTHROPLASTY OF THE HIP FOR OSTEOARTHRITIS UTILIZING FOREIGN-BODY CUPS OF PLASTIC

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THIS presentation will deal with two subjects: arthroplasty utilizing foreign substances of nonanimal origin and end-results of these and other methods in ameliorating pain and disability in osteoarthritis of the hip. Péan and Chlumsky were the first to utilize foreign materials in arthroplasty, the former in human joints, while the latter experimented with an array of metal plates and films of celluloid, rubber, and collodion. Sir Robert Jones, utilized a strip of gold foil to cover the reconstructed head of the femur. He reported 21 years later that motion was still present in the reconstructed joint. Pupovac reported the temporary success of a magnesium plate in an arthroplasty. Rehn, however, appears to be the first to grasp the principles of a cup arthroplasty when he inserted into the hip a previously molded cap-like appliance of steel, spiked upon the acetabular side. This appliance was removed 8 weeks after the first operation. At this second stage he interposed an autogenous graft of fat and fascia. Smith-Peterson (45) has utilized cups of various materials: glass, viscaloid, pyrex glass, bakelite, prior to his adoption of vitallium cups. While he appears not to have further explored the possibilities of nonmetallic cups, bakelite was apparently satisfactory in 1 case, as he wrote that "the mold is still in place (2 years after the operation) and the patient is doing well." The disease for which this operation was performed and the ranges of preoperative and postoperative motion were not given. Payr and the MacAuslands have summarized the subject of arthroplasty in their books.

The successful application of the cup principle to arthroplasty of the hip came with the utilization in surgery of the newer metal alloys, especially vitallium. Hopkins and Zuck reported the first use of a vitallium cup for hip joint arthroplasty in a patient suffering from osteoarthritis of this joint following trauma. Smith-Peterson (45) reported upon the use of a flanged vitallium cup, and at about the same time Venable and Stuck reported upon a mold of this same metal which they affixed to the femoral head. Smith-Peterson's cup is allowed to remain more or less free, being attached neither to the femoral head nor to the acetabulum, while its small everted rim anchors it loosely in the acetabulum. Its shape would lead one to believe that the majority of motion is secured between the mold and the femoral head. Venable and Stuck fix their cup to the femoral head and neck by a vitallium screw. Another technical variation has been introduced by Preston who uses a flanged cup fixed to the contour of the acetabular margin by an irregular rim. Further discussion of the desirable shape for the hip cup will appear in a later section of this paper.

In recent years many individual reports of arthroplastic operations upon the hip have appeared in the surgical literature. These have been quoted and summarized elsewhere (MacAusland and MacAusland, Murphy, and Payr) and, in the main, are of historical interest only, contributing little to modern conceptions of arthroplasty. Reports of end-results, following hip arthroplasty for osteoarthritis in which autogenous fascia lata was used, are of interest in establishing a standard for comparison to the cases reported herein. Campbell (7) stated that he had obtained 60 per cent good results in his cases, but a later detailed analysis of his cases, even though not classified according to the present accepted nomenclature for arthritis, leaves the impression that the percentage of satisfactory results was not as great in persons suffering from "chronic arthritis." Hallock (11) reported on the end-results of 70 arthroplasties and reconstruction operations upon the hip joint, of which 24 were cases of osteoarthritis of this joint. In this group of cases pain was considerably alleviated but average motion was lost. This author indicated that the results were "much better" when proper selection of cases and newer operative principles obtained. Fuiks reported the end-results from single layer autogenous fascia lata arthroplasties in 60 patients operated upon in Steindler's clinic. Of these cases, 15 were instances of osteoarthritis of the hip. The results were de-

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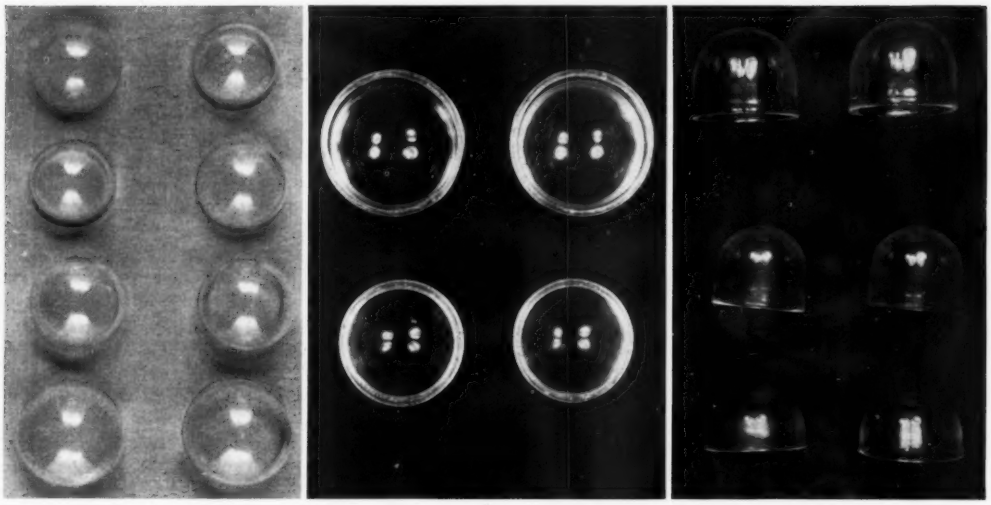

a b c

Fig. 1. Types of methacrylate cups for hip-joint arthroplasty. a, An assembly of plain cups of approved size. The three smallest sizes serve for the majority of patients. b, Cups having a heavy stainless steel wire in the rim. These cups orient the observer in roentgen studies. c, Long and short cups. The long cups inhibit motion and are not preferred.

scribed as "good," in 46 per cent, and "fair," in 40 per cent, a total of 86 per cent. The significance of a "good" result was one in which there was "at least 45 degrees of flexion and no pain." The results were "classified as fair when there was less than 45 degrees but more than 20 degrees of motion, and the patient had little or no pain and was personally well satisfied with the result, either because of decreased pain, increased motion, or better position of the limbs." In our experience the final results vary, depending upon the original motion prior to operation upon the osteoarthritic hip. This factor was not considered by any of the previous authors in reporting end-results.

While vitallium is desirable for this purpose because it is electrically inert in the tissues, it possesses, like any metal the unfavorable property of being radio-opaque. Changes in the femoral head stump, which are known to occur with frequency following membrane arthroplasty, cannot be visualized through this metallic foreign body. Aseptic necrosis of the femoral head probably occurs, in a certain percentage of cases, following cup arthroplasty. Indeed, Ferguson states that it is not possible to remove more than one-third of the circumference of the femoral head (in arthroplastic procedures) because absorption of the remaining portion will often occur (due to aseptic necrosis and pressure destruction.) Some of the indifferent results that have occurred following the use of vitallium cups may be due to proliferation of new bone about the acetabular rim or from the femoral neck around the cup margins, or to aseptic and pressure necrosis of the remodeled femoral stump (2, 35, 36, 40). Pain, present in a certain percentage of cases in which metal cups are used, may possibly be due to the hardness of the weight bearing surface.

In searching for a material (16, 17) that would possess the property of radiotransparency and still be well tolerated by the tissues, the author's attention was directed to the group of plastic materials which have come into recent general use in industry. From a consideration of physical properties the methacrylate resins (lucite and plexiglass) and the polystyrenes were selected. The methacrylate plastics[1,2] only were used in the cases reported in this paper. These substances are polymers of methyl methacrylate. When cast in rods, sheets, or blocks, the material is crystal clear, light in weight (specific gravity, 1.18) and slightly flexible, but is also durable and strong as evidenced by the following physical constants: tensile strength, 9,000 to 12,000 pounds per square inch; flexural strength, 12,000 to

[1]From a description of "lucite," a new DuPont plastic material for industrial use, E. I. DuPont DeNemours and Company. Plexiglass, (Röhm and Haas Company) is another methacrylate plastic.

[2]Plastic cups utilized in this report have been manufactured by molding from methyl methacrylate sheet (lucite, plexiglass, etc.).

a b c

Fig. 2. Early changes of osteoarthritis in the hip. a, Hips of a young man of 33 years. Advanced changes in one hip and early changes in the contralateral hip. The latter, although asymptomatic and having normal joint space, demonstrates early osteophyte formation on the anterior and superior neck and the early inferior adductor atrophy and osteophyte formation. b, A stage slightly more advanced. In addition to the early stages noted in, a, supra-acetabular and femoral head sclerosis is present. c, Another type of early change consisting of a wedge-shaped osseous infarct, which has undergone retransformation into living bone at its base. Pain, however, without limitation of motion, was present in the case of this patient.

14,000 pounds per square inch; impact resistance, 0.1 to 0.3 foot-pound; hardness (Brinell) 500 kilograms on 10 millimeter ball, 17–20. It may be cut, turned, sawed, carved, drilled, polished, shaped, formed, and swaged. It has a negligible water absorption since less than 0.5 per cent by weight is absorbed upon immersion for 7 days, and is resistant to sun and ordinary atmospheric exposure. Solid methacrylate is not affected by alkalies, oils, dilute acids, solutions of mineral salts, and dilute alcohol.

Cast methacrylate will not soften until 190 to 240 degrees F. has been reached, while moldings will withstand 140 to 190 degrees F., depending upon whether prepared from "soft" or "hard" powder. The polystyrene plastics are similarly resistant. Both these substances retain only traces of irritating solvents called "plasticizers" in industry, while the phenolic plastics retain appreciable amounts of these materials. For our purposes, the methacrylate hemispheric cups were sterilized by prolonged (1 hour) immersion in a 0.2 per cent solution of mercuric oxycyanide, followed by rinsing in sterile distilled water. Mercuric chloride solution (0.1 per cent) has also been used. Figure 1 shows an assembly of plastic cups. The two small cups were found to fit the trimmed femoral heads in the majority of cases. The walls of the cups were 3/32 and 3/16 inches thick and the cup itself was molded into hemispheric shape. The radius of depth of these cups was less than their internal cross-sectional radius (¾ and ⅞ inches). The two larger cups, used infrequently, had an internal cross-sectional radius of 15/16 and 1 inch, respectively.

ANATOMY OF THE HIP

The conventional conception of the normal hip as a "ball and socket joint" is inadequate. The normal femoral head represents about two-thirds of a true sphere, the circular cross-sectional base of which becomes continuous with a near cylindrical femoral neck, which structure bulges on either end. The center of curvature of the portion of the sphere that is the femoral head does not lie in the plane of junction of head and femoral neck, but in a plane about one-third of the distance between the plane of junction of head and neck and a tangential peripheral plane that passes through the central fovea of the head. The aim of the cup arthroplasty, to be described later, is to decrease the enlarged volume of the irregular osteoarthritic femoral head, to restore a presenting true spherical surface, and to cap it with the hollow plastic hemisphere. A true sphere is the only presenting surface that will not further restrict motion. Cup-like molds, whose radius of depth exceeds the maximal cross-section radius (Fig. 1c), further restrict motion by impingement of the excess length of the cup margins upon the femoral neck and acetabular margins. This fact has been verified at operation upon many occasions.

The acetabular margins are higher superiorly and posteriorly and are defective in an inferior (acetabular) notch, covered in the living by transverse ligaments. The acetabular cavity presents laterally and inferiorly. The interior of the acetabulum is far from being a true "socket" or "cup." The superior and posterior roof contains a slightly elevated condensation of osseous articu-

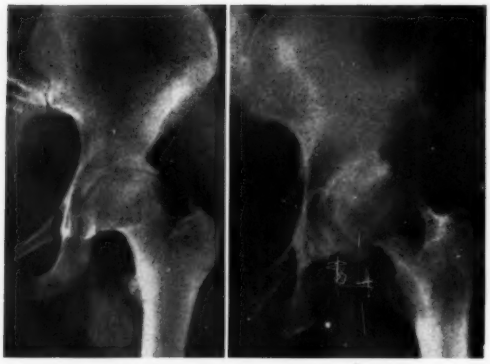

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Fig. 3. Moderately advanced changes of osteoarthritis of the hip. a, Shows narrowing of joint space, osteophyte production on both femoral head and acetabulum and sclerosis within the head. These changes were secondary to pyogenic arthritis of the hip many years before. b, Changes within the head and marked mirror-like osteophyte formation in the adductor region of both acetabulum and femoral head. Supra-acetabular sclerosis is more marked than in, a.

lar cortex not exceeding one-third to one-half of the total interior surface of the acetabulum. This prominent and raised osseous portion represents the weight bearing zone of the acetabulum and is visualized in the conventional anteroposterior roentgenograms as the "acetabular roof." The articular cartilage fills in the remainder of the acetabulum with the exception of the fovea. In the living normal hip the presenting acetabular surface is smooth, the cartilage covering the weight bearing osseous surfaces being thinner than elsewhere. The variations of the structures that are encountered in operative surgery upon the osteoarthritic hip will be described in the following section.

The normal adult femoral head varies in diameter, being largest in the male. The few direct measurements that have been made at operation indicate the normal diameter to be between 1⅝ and 2 inches. The largest male femoral heads may even approximate 2⅛ inches, while the smallest female heads may have a diameter approximating the first mentioned figure; some are as small as 1½ inches. Even though considerable variation has been encountered in the femoral head, the transverse diameter of the femoral neck at the midpoint between its junction with the head and the cervicotrochanteric junction is almost constant at ⅞ inch with maximal variations of 1/16 inch. A fair approximation of the osseous femoral head may be obtained from roentgenograms, when the distortion factor of approximately 0.9 at a 3 foot tube distance, and an 8 centimeter object to film distance are borne in mind.

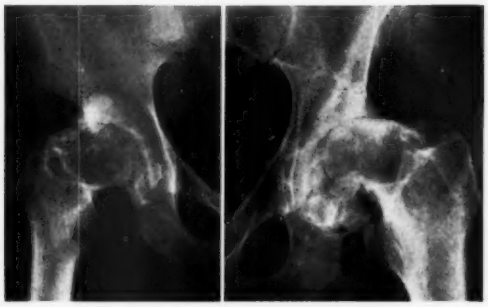

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Fig. 4. Advanced changes of osteoarthritis of the hip. a, One hip of a case secondary to bilaterally congenital inadequate acetabula without dislocation. "Cysts" are seen within the head, a large adductor femoral head osteophyte and sclerosis and new bone formation in the superior portion of the joint. b, Single hip from another bilateral case (primary). This demonstrates, in addition to other changes, a gigantic ramifying adductor osteophyte.

GROSS AND MICROSCOPIC ALTERATIONS OF THE OSTEOARTHRITIC FEMORAL HEAD

The following description is based upon the study of roentgenograms of 94 osteoarthritic hips from the files of the Guthrie Clinic and the Robert Packer Hospital and from the direct observation of approximately 60 osteoarthritic hips at operation, including those reported herein. The histories presented by the patients are considered in the succeeding section dealing with "etiology and pathogenesis of osteoarthritis" of the hip and in the appended case reports.

The changes to be seen in roentgenograms of the "early osteoarthritic hip" (Figs. 2a and 2b) include marginal osteophytes at the head-neck junction or at the lateral acetabular margin, widening of the head by growth of the adductor portion of the head, as seen in the anteroposterior film, and sclerosis within the head and above the acetabular articular bony cortex (supra-acetabular sclerosis). At this time the superior "joint space" (cartilage space) may be normal or slightly diminished (Fig. 3). As further changes take place, spotty sclerosis appears in the head (Figs. 2b, 3a and b) (denoting osseous infarction or endosteal proliferation). Marginal osteophytes increase in size and especially the adductor portion of the head becomes disproportionate. In advanced cases the adductor osteophyte may be half as large as the head itself (Fig. 4b) and may

a b

c

Fig. 5. Cases illustrating the pathogenesis of secondary osteoarthritis of the hip. a, Case secondary to changes in the femoral head associated with fracture of the mesial acetabular wall with minimal displacement of the fracture fragments. a^1, 22 months after fracture and a^2 48 months following fracture. Note new bone production on the mesial acetabular wall, transformation of a superior femoral infarct with sclerosis about the area of transformation. b, Stages in necrosis and transformation of a femoral head produced by a fracture at the base of the neck. During these spontaneous changes the patient was kept from weight bearing, resulting in preservation of cartilage. b^1 6 months after fracture, and b^2 35 months following fracture. c, Delayed necrosis in the femoral head following internal fixation for transcervical fracture with a Smith-Petersen pin. This complication occurs in 10 to 20 per cent of such fractures and develops gradually within the first 2 years following fracture. This roentgenogram was taken 23 months after the fracture and fixation.

cause partial dislocation of the head. This portion of the head may render the femoral head egg-shaped and be a major factor in causing the head to be difficult to dislocate at operation and in restricting motion of the joint. The head increases in size both by subchondral sclerosis and by its enlargement by osteophytic proliferation as just described. Subchondral sclerosis is accompanied or preceded by the changes in cartilage as will be described. As a result, irregular islands of cartilage thinning occur, which in advanced stages may bare subchondral bone. Cartilage is thrown up into pleat and ridge formation, the whole giving the head an irregular appearance. The extent of marginal overgrowth of bone and cartilage never parallels the rate of degeneration of cartilage over the head and of actual enlargement of the osseous structure of the head. Consequently, osteoarthritic femoral heads are never identical.

Most of the alterations which are seen in the customary anteroposterior roentgenograms of the hip and which appear to be acetabular osseous overgrowths are actually alterations on or in the femoral head (Figs. 4b and 11a). Indeed, such roentgenograms seldom give an accurate impression of the relative changes on the femoral head and acetabulum as actually visualized at operation. Little or no removal of marginal overgrowths on the acetabulum is required except in advanced cases and then only from the anterior and anteroinferior portion of the acetabulum. Lateral views of hip with leg abducted and externally rotated are of help in visualizing the extent of relative involvement of femoral head prior to operation.

Avascular necrosis (2, 12, 21, 24, 26, 39, and 43) plays an important rôle in either initiating change in cartilage or else takes place in the femoral head after initial cartilage damage. All femoral heads visualized and trimmed at operation in this series contained greater or smaller islands of osseous infarction. The arrangement of these islands was often such as to suggest that wedge-shaped infarction either initiated the osteoarthritic changes or appeared at an early date in its course and contributed significantly to its advancement.

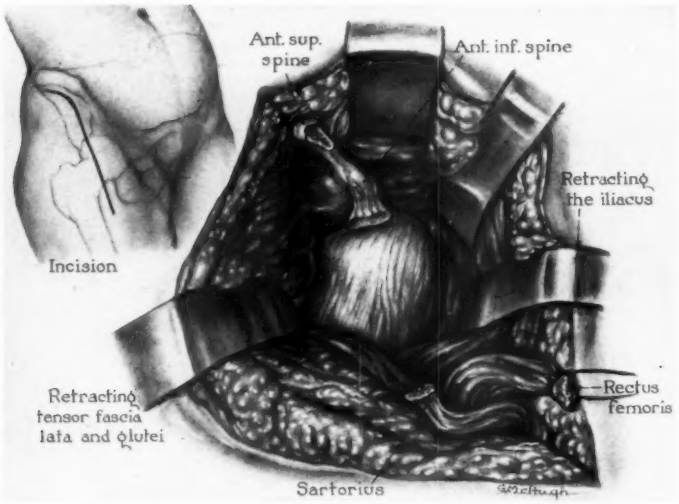


Fig. 6. Incision and precapsular dissection in exposure of the movable osteoarthritic hip.

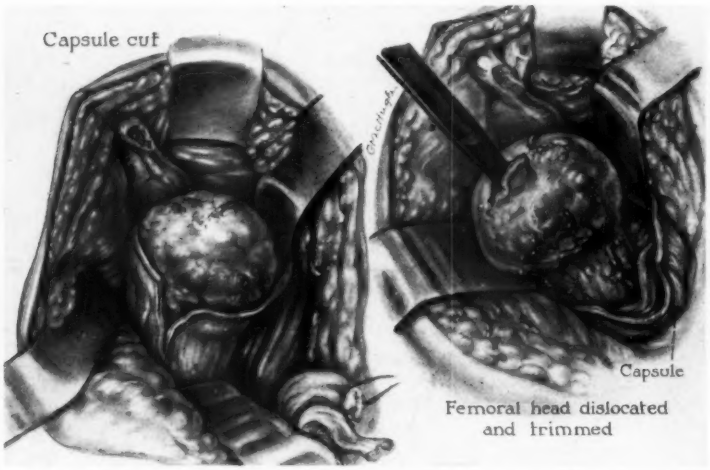


Fig. 7. Dislocation and trimming of the enlarged and irregular osteoarthritic femoral head.

The ligamentum teres is usually reduced to a small fibrous cord and often only projects as a scarred remnant on the head and from the central portion of the acetabulum. In only 1 of 25 cases did blood ooze from the remnant. This fact probably accounts for some of the avascular necrosis of the osteoarthritic femoral head and at the same time explains why further necrosis of the femoral head is rarely seen after arthroplastic operations upon the osteoarthritic femoral head which necessitates dislocation of this structure.

The fundamental lesion in osteoarthritis or degenerative arthritis is the change that takes place in the articular cartilage. Whether osseous infarction occurs first or cartilage degeneration precedes it is immaterial as the end-result is the same: degeneration and fibrillation of cartilage and thickening and sclerosis of subchondral bone.

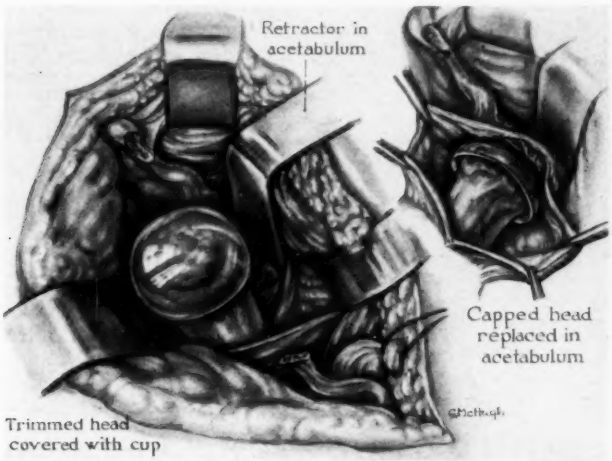


Fig. 8. Capping the trimmed head and replacement of it into the acetabulum.

These changes have been described by Axhausen, Phemister (34, 36), Kistler, Lang (24, 26), and others, to whose writings the reader is referred for details. The first change in the articular cartilage is a change in the staining reactions of the matrix which is the familiar gross increase in translucency and change in color. The matrix then becomes fibrillated, the direction of the cartilage pits being both vertical and horizontal. Deposits of calcium are seen in the cartilage, and pleats and cavities appear in the cartilage. The usual orderly arrangement of cartilage cells in articular cartilage is superceded by a "disordered appearance," and the viable cells are placed in an abnormal fibrous matrix. All transitions can be seen at times between normal cartilage and fibrocartilage.

Continued irritation of movement is probably responsible in some degree for changes that take place in subchondral bone. Beneath areas of cartilage change, osseous trabeculae thicken by appositional growth of osteoid tissue. The osseous subchondral plate itself thickens by the same process. Bony sclerosis also occurs by the process of enchondral ossification under areas that are better protected by cartilage. Proliferation of bone by the process just described occurs at the margins of the joint, and pushes cartilage before it, thus forming marginal osteophytes. The eburnated and polished appearance of subchondral bone is due to the tremendous thickening of this latter structure in addition to the polish it acquires by friction. Elsewhere, especially at some depth beneath the osseous cortex, the trabecular pattern is thinned, and cyst-like structures containing fatty tissue are seen. Other cyst-like cavities (Fig. 4a) are seen lined by fibrous tissue. The preponderance of these latter structures in certain cases has been responsible for the roentgenologist introducing the descriptive term of "senile cystic arthritis." It is but a type of degenerative arthritis.

ETIOLOGY AND PATHOGENESIS OF OSTEOARTHRITIS

Thirty-seven, or 39.4 per cent, of the 94 patients upon whom records were available at the Guthrie Clinic and the Robert Packer Hospital, could be assigned to the group of secondary osteoarthritis (Figs. 3, 4, and 5). The remainder, including many in which wedge-shaped infarcts of the femoral head were present, was classed as primary. It is possible that, if roentgenograms had been made at earlier dates in some of the latter cases, many would have been placed in the category of secondary cases. The causes of secondary osteoarthritis of the hip are given in Table I, and some illustrations of this type are shown in Figures 2 to 5. These findings are in agreement with those of Plewes, Gilmour (14), and Wiberg. The first mentioned, in reviewing 242 cases from an English orthopedic hospital, found that in 47.9 per cent of his cases a definite preliminary disorder, often an adolescent hip joint disease, had caused enough damage to be later followed by osteoarthritis. Presumably the

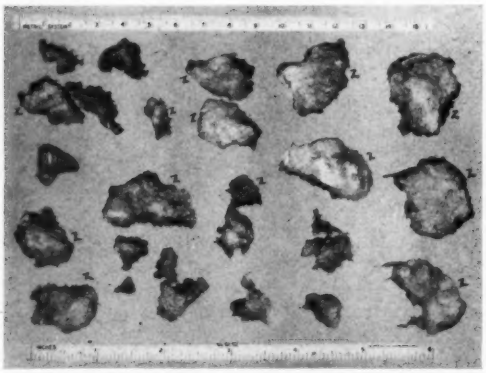


Fig. 9. Case 4. Bone removed from the femoral head in the arthroplastic operation described in this report. The weight of these specimens varies from 50 to 80 grams. *z* designates osseous fragments bearing remains of articular cartilage. Note pits and ridges.

early mechanical derangement subjected the hip to unusual weight bearing stress and caused early cartilage degeneration and the other changes previously described.

The mean age in the group of patients with primary osteoarthritis of the hip was 64 years while that of the secondary cases was 45 years. The incidence of osteoarthritic changes in other joints in the first group was four times as common as in the group of secondary cases. The disease was unilateral in all the secondary cases, except those following protrusio acetabuli (Fig. 15c), rheumatoid arthritis, Paget's disease, and slipped upper femoral epiphysis (Fig. 11a). Obesity of a significant degree was present in one-third of the cases, and the body build in almost all the patients, females included, could be described as "large." Foci of infection, generalized arteriosclerosis, cardiac disease, anemia, and increase in the blood sedimentation rate were encountered occasionally but not with a frequency that would implicate them as causative of the condition. Indeed, save for the joint condition, the majority of these patients were in unusually good physical condition. All facts served to point to a degenerative disease of the hip, often preceded by a disorder that then subjected this structure to mechanical disadvantage. The bony changes that were encountered are the reactive changes in a joint that continues in use following initial damage. Magnuson and others have reached a similar conclusion in studying other joints affected with osteoarthritis.

OPERATIVE TECHNIQUE

When the hip joint is opened for an arthroplastic procedure in the presence of a movable joint, it is not necessary to carry out as radical a dissection as is necessary when this joint is almost totally or completely ankylosed. In the instance of total osseous ankylosis as encountered in the end-stages of pyogenic arthritis of the hip joint or instances of ankylosis from the Marie-Strümpel

a b c

Fig. 10. Roentgenograms of the hip of Case 1. a, Preoperative, showing sclerosis, diminished joint space and a small projecting adductor osteophyte that articulated with a similar acetabular overgrowth and blocked abduction and rotation. b, Six months after operation. A portion of infarcted bone in the superior portion of the head was noted. At operation this bone had been noted but there was no evidence of its separation. c, Eighteen months after operation. Note changes in the head and that the infarcted bone has separated and now lies in the inferior portion of the joint. The patient's motion has been maintained and he has had no pain or locking of the joint.

TABLE I.—CAUSES OF SECONDARY OSTEOARTHRITIS OF THE HIP

Juvenile and adolescent
- Coxa plana (Legg-Calvé-Perthes' disease)
- Slipped (or slipping) upper femoral epiphysis
- Septic arthritis (with or without dislocation)
- Childhood arthritis (Still's disease)
- Congenital dislocation of the hip (with or without operation and/or reduction)
- Congenitally inadequate acetabulum
- Congenital anomalies of the upper femur
- Coxa vara of other types (rickets, osteomalacia, etc.)

Adult
- Injury (followed by aseptic necrosis in femoral head)
- Fracture of the pelvis into the acetabulum
- Fracture of the femoral neck
- Traumatic dislocation, complicated by late avascular necrosis
- Rheumatoid arthritis
- Septic arthritis
- Protrusio acetabuli (Otto pelvis), traumatic or infectious in origin
- Paget's disease of pelvis and upper femur
- Caisson disease
- Chondromatosis and osteochondritis dissecans
- Lues (painless "Charcot" hips)

a b

Fig. 11. a, Preoperative roentgenogram of Case 6, secondary osteoarthritis following an adolescent slipped upper femoral epiphysis and aseptic necrosis in the femoral head. Motion at this time was limited to flexion only. b, Roentgenograms 6 months after operation. Note the improved mechanical condition of the hip and that nearly all excess bone was on the femoral head.

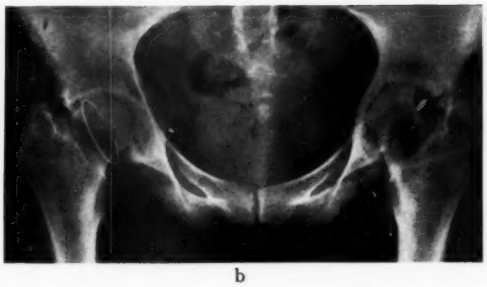
type of atrophic arthritis, the partial intrapelvic approach recently described by Smith-Peterson (44) should be used. It is seldom necessary to make such an extensive dissection in patients upon whom arthroplasty is being performed for osteoarthritis.

The technique recommended requires minimal detachment of muscles since it is felt that hip-joint motion is only further weakened by extensive dissection. An 8 to 10 inch horizontal incision is made in the upper anterior thigh, the upper 2 inches of which curves outward from the anterior superior iliac spine, along the anterior iliac crest (Fig. 6, inset). This latter structure is exposed, and the subcutaneous incision is extended downward along the outer border of the sartorius muscle. The upper 4 inches of the sartorious is defined, its origin removed, together with a fragment of cortical bone, from the anterior superior iliac spine. A portion of the origin of the tensor fascia lata and the extreme lowermost fibers of origin of the gluteus minimus are detached by subperiosteal dissection from the lower anterior iliac crest. Care should be taken to detach only the minimum of muscle in this last maneuver; it is never necessary to detach the fibers of the gluteus medius when the hip remains movable. The total length of the muscle detached from the iliac crest never need exceed 2 inches and is often less. By retracting the detached sartorius downward in the wound, the anterior inferior iliac spine is exposed, and the origin of the tendinous head of the rectus femoris is defined. It is then

a b c d e f

Fig. 12. Photographs illustrating the range of active motion 9 months following operation in Case 6. a, Internal rotation; b, external rotation; c, abduction; d, flexion; e, bending; f, squatting.

a



b

c

Fig. 13. a, Preoperative roentgenogram of the pelvis of Case 8, bilateral primary (?) osteoarthritis of both hips. The acetabulum has some characteristics of arthrokatydiasis (Otto's pelvis), which is discernible to better effect in b, the postoperative roentgenogram, taken 3 months after the operation; c, roentgenogram of the left hip, 15 months following cup arthroplasty, showing collapse (partial) of the head-neck stump under weight bearing.

detached by cutting through the tendon. The distal free tendinous edge is anchored to the lower wound margin by transfixing it three or four times by a through and through stitch of No. 1 or 2 chromic catgut and stitching it loosely and temporarily into the lower angle of the wound. This same stitch is later used to reattach the divided tendon of the rectus femoris upon conclusion of the operation.

The accurate placement of retractors at this point gives complete exposure of the anterior and superior portions of the hip-joint capsule. Both bands of the iliofemoral ligament should be visible in their entire course. The iliacus is retracted mesially with a broad retractor, the tensor fascia femoris laterally and posteriorly, and the gluteus minimus and the lower border of the gluteus medius superiorly. The detached sartorius and rectus femoris are in the inferior angle of the wound (Fig. 6). The ascending terminal branch and at times the transverse terminal branch of the lateral circumflex artery are usually exposed. Time is conserved and better hemostasis is obtained by dividing and ligating the vessels if they lie near or over the anterior aspect of the hip-joint capsule. There is much variation in the origin, course, and branches of the lateral circumflex artery, but they can be visualized. The capsule is then opened by a crucial incision. The extent of periacetabular new bone is noted, and the necessary amount is removed from the anterior acetabular margin. The femoral head is then dislocated. This maneuver is facilitated by driving a slightly curved broad bladed osteotome into the anterior aspect of the joint between head and acetabulum. The operator levers the head out while an assistant manipulates it externally. Both the femoral head and the interior of the acetabulum are then thoroughly inspected and the extent and nature of the pathological changes are noted. The ligamentum teres will usually be found absent or represented by a well compressed fibrous cord. Cartilage destruction is usually most accentuated on the weight bearing portion of the femoral head, and is usually farther advanced over the femoral head than in the acetabulum. When osteophytic bone is the prominent feature of the pathological process, it is distributed circumferentially about the femoral head, extending distally back over the neck, especially on the superior and anterior aspects, where cortical bone of the neck is often obscured. The head in osteoarthritis is usually distorted in shape by osteophytes especially the adductor enlargement which is an almost constant and important part of the pathological picture.

The femoral head should be reduced to a volume definitely smaller than normal circumferential size. Often one-third to one-half of the mass of the pathological femoral head is removed inasmuch as it usually is increased in size (Figs. 7, 10, and 11). The amount of bone removed averages from 50 to 80 grams. Osteophytes are trimmed from the head-neck margins, a plane of division being easily found between these new-growths and the normal cortical bone of the neck. All types of osteophytic variations will be found from a marginal ring at the head-neck margin to gigantic osteophytes that bridge the entire neck and are contiguous with trochanteric bone. When wedge-shaped areas of osseous necrosis are present in the femoral head, they are easily recognized by the yellow avascular appearance contrasting to bleeding bone about them. The head is reshaped without special attention to them, except to reduce the total head volume to the minimum in this special instance and thus to shorten the longitudinal neck diameter. Care must be taken to trim the head symmetrically in relation to the neck, since the osteoarthritic changes have usually rendered it asymmetrical.

Periacetabular osteophytes are removed by a curved chisel from an extra-acetabular approach. Since they frequently develop in the origin of the iliofemoral and pubocapsular ligaments, portions of the acetabular attachments of these ligaments are frequently torn in their removal. No special attempt is made to reattach the ligaments. If the detachment is extensive, portions of the ligaments are excised, but since removal of periacetabular bone is seldom extensive, a fair reconstruction of the capsule can be obtained and is recommended. The acetabular surface is not attacked unless it is extensively ridged by cartilage pleats and by islands of surviving cartilage, in which case, the osteocartilaginous surface is carefully smoothed by shaving off excess cartilage. Bone removed and some of the surface changes are illustrated in Figure 9.

The presenting and raw osseous surface of the reduced femoral head is then smoothed with the cup reamer and capped by a loosely fitting methacrylate hemisphere. In most of our cases, the two smaller size cups were the best fits. Care should be exercised that the cup is quite loose over the head and that the cup does not bind in the acetabulum after reduction of the dislocated head (Fig. 8). The capsule is then closed loosely with interrupted fine cotton sutures. The muscles are reattached with the same suture material, the deep fascia is closed with interrupted cotton sutures, and the subcutaneous tissues is approximated by the same method, with care to bury the knots well beneath the skin. The skin can then be approximated by any of the recognized methods.

a b

Fig. 14. a, Preoperative roentgenogram of Case 9, osteoarthritis secondary to possible juvenile pyogenic arthritis. In this instance the new bone is both acetabular and from the head-neck junction. Note the large superior osteophyte and the moderate sized adductor osteophyte. b, Postoperative roentgenogram. Note that the acetabulum is deformed, its cavity opening more anteriorly than anteroinferiorly.

POSTOPERATIVE TREATMENT

For the first 2 to 3 weeks the limb is held by an internal rotation strap of broad adhesive and by Buck's extension (7 pounds) applied to the leg. The balanced Hodgen or Thomas splint with a Pearson attachment can be used for limited active and passive motion to both hip and knee. Both are started within a few days after operation, as soon as the muscle and wound tenderness will permit. During the third week, Buck's extension is used intermittently for a week and the patient is up in a wheel chair and begins systematic exercise in the physiotherapy department. Active and passive exercises are then given daily for both hip and knee. The patient is instructed to devote 10 minutes of every waking hour to combinations of quadriceps setting exercises, and active flexion and abduction of the hip. There is no danger of dislocation of the hip. The patient is allowed to walk with the aid of crutches, supporting body weight largely on the normal leg, from 25 to 28 days after operation. Full weight bearing

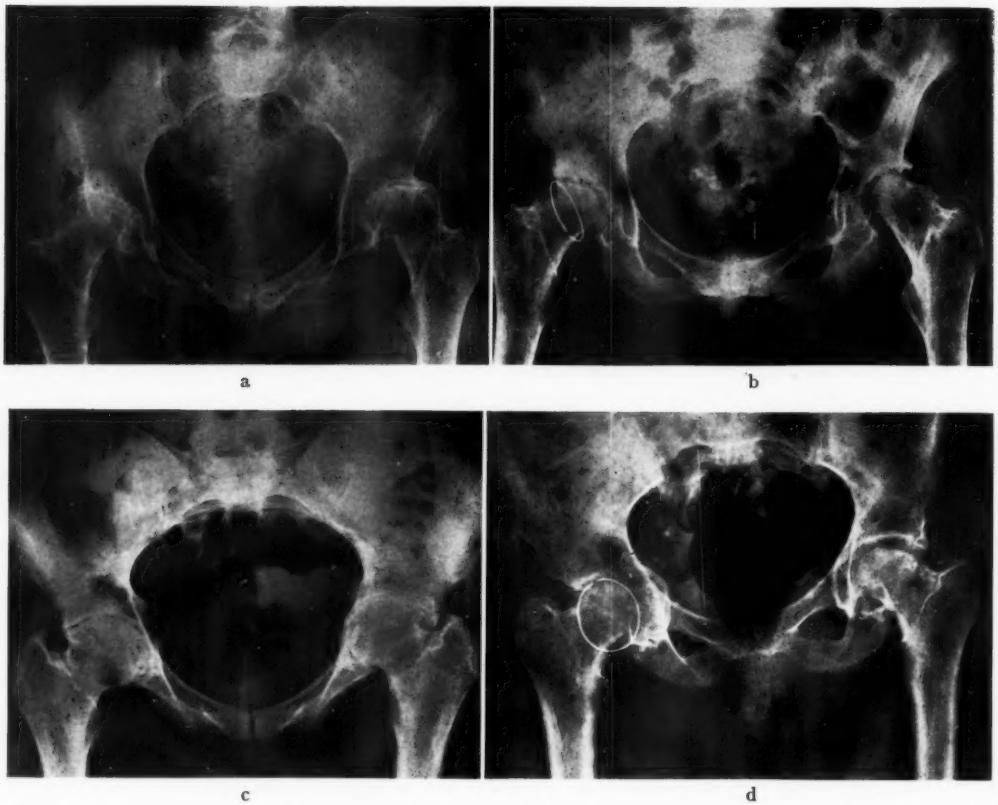


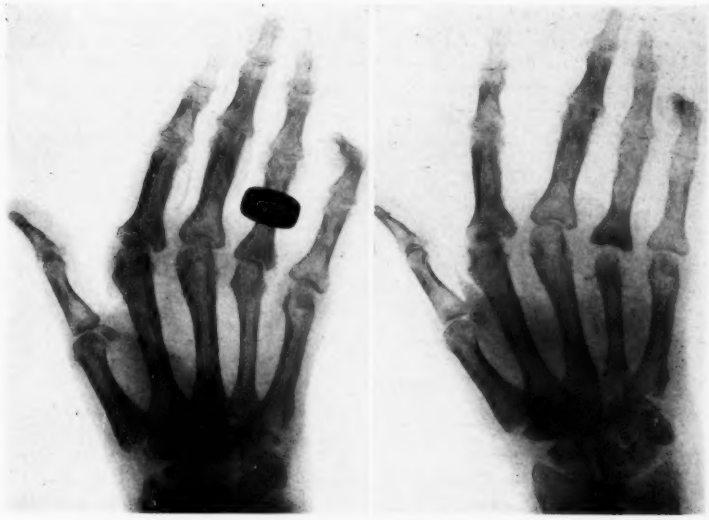
Fig. 15. Preoperative and postoperative roentgenograms from two additional bilateral cases—Cases 11 and 13. a and c, are preoperative while b and d are films taken following operation.

on the operated leg is allowed, still with crutches, 4 to 7 weeks after operation. The patient is requested to continue to use crutches until he has full confidence in the strength of the hip that has been operated upon. The use of crutches is insisted upon for 3 months following operation upon a single hip, but upon request some of the patients have not discarded them until 4 or 5 months after operation. Careful postoperative manipulation is occasionally used to increase motion but the majority of cases do not need it. It should always be performed gently. When both hips are operated upon in the same patient, the second hip is usually done some 10 days to 2 weeks after the first. With the patient in bed physical therapy is then given to the hip joint first operated upon until the second hip is removed temporarily from traction. After the 4th week in the case of unilateral operations and the 6th week in bilateral operations, strenuous exercise upon the inclined plane and upon the exercising bicycle is given.

REPORT OF CASES[1]

CASE 1. Male, aged 60 years, suffered from osteoarthritis of the left hip for 12 years prior to treatment at the Robert Packer Hospital and Guthrie Clinic. Marked pain was present in the left hip during the year prior to operation. The limit of his endurance in walking was one or two blocks. At operation a plastic cup was inserted in the left hip and the femoral head was reduced one-third in volume. The patient's postoperative course was uneventful but he continued to use crutches, on our recommendation, for 4 months. The postoperative range of passive motion was double that prior to operation. From the 6th month, the patient stated that he could walk 3 to 5 miles daily without pain. During the changeable winter months, however, he complained of "muscle soreness" of slight degree in the left thigh (referred pain). It was considered that this patient had almost complete relief from pain. Roentgenograms of the patient are reproduced in Figure 10.

[1]Table II shows for all cases range of passive motion before and after operation. (Active motion, as a rule, was three-fourths passive).



a b

Fig. 16. Roentgenograms before, a, and after operation, b. Note the restoration of joint space and the trimmed distal fourth metacarpal head in the latter view.

CASE 2. Male, aged 60 years, suffered from multiple osteoarthritis chiefly affecting the lumbar spine and the left hip, although there were definite changes in the right hip and in both knees. The duration of this process was 2 to 4 years prior to operation. In the 4 months prior to operation he had had 6 or 7 acute attacks of pain in the right hip which necessitated his being off work for several days on each occasion. At operation on the right hip, marked changes of degenerative osteoarthritis and many marginal osteophytes were found on the head. The bone of the femoral head was eburnated and avascular, the latter changes extending into the head in multiple wedges. One-third of the entire mass of the head was trimmed away, with no attention to the distribution of avascular bone. The hypertrophied superior and anterior ledges of the acetabulum were removed with a chisel from an intracapsular approach. In this case the remains of the ligamentum teres were present and a slight ooze was identified from the proximal end of this structure, after dislocation. Following operation, the patient has never been able to walk without his crutches, except in his house. He has had two or three attacks of pain in the opposite hip and in both knees, although the hip on which the arthroplasty was performed has been the site of greatly increased motion and he has been relieved of pain in this hip.

This case is now considered as being an error in selection (age, poor muscle strength, and multiple osteoarthritic involvement, the symptoms of which are moderately active at the present time).

CASE 3. Male, aged 40 years, dated the onset of his disability to World War I. While in the armed forces he received an injury to his hip without fracture. He had always had some pain and disability in the hip during the 20 years succeeding the injury, but these symptoms had become gradually worse during the 4 or 5 years prior to being seen at the Guthrie Clinic and the Robert Packer Hospital. Roentgenograms showed far advanced osteoarthritis of the left hip (secondary). The joint space was almost completely obliterated and there were large osteophytes both on the margins of the acetabulum and the femoral head, as well as sclerosis and small cysts within the head. During the immediate 1 year prior to operation the pain had been considerable most of the time and had forced the patient to resort to alcohol and to crutches for relief. At operation, a large number of periacetabular osteophytes were seen and removed, especially from the anterior and inferior margins of the acetabulum. The bone of the head and trochanter was united over the anterosuperior portion of the trochanter by an osseous bridge. It was estimated that the head was trimmed to one-half its previous proportions. The weight of the bone removed at operation was 82 grams. In the outer third of the head a large quantity of avascular bone was encountered during the trimming process. The head was then capped with a plastic cup, after it had been smoothed with a female reamer. Following operation, the patient progressed according to schedule and was discharged 5 weeks after operation. Further postoperative course was ideal, except for one bout of an acute exacerbation in the right hip occurring 4 months after operation. At that time, against our advice, he had gone without his crutches for 2 weeks and had participated in some unusual exercises. The pain again disappeared following great restriction in his activities. Fourteen months after operation the patient reported, on a follow-up visit, that he was on his feet 8 to 12 hours per day and suffered no pain. Active motion was about 7/8 of the range of passive motion (Table II).

CASE 4. Female, aged 64 years, had begun to suffer pain in the right knee (referred pain from the right hip) 8 years prior to admission to the Guthrie Clinic and the Robert Packer Hospital. On admission the patient had markedly restricted motion at the right hip (Table II) which was

TABLE II.—RANGES OF PASSIVE MOTION AT THE HIP JOINT BEFORE AND AFTER METHACRYLATE CUP ARTHROPLASTIES

(in degrees, from neutral position; time postoperatively in months)

Case No.	Sex Age		Flexion	Extension	Total adduction Total abduction	Rotation	Comparative result
1	M 60	Preoperative	30	15	25	10	Excellent
		Postoperative (28 mo.)	60	30	50	20	
2	M 60	Preoperative	70	0	0	0	
		Postoperative (26 mo.)	90	20	55	20	Poor
3	M 40	Preoperative	60	10	0	0	
		Postoperative (24 mo.)	90	20	110	90	Excellent
4	F 64	Preoperative	30	0	0	0	
		Preoperative (anesth)	80	10	30	15	
		Postoperative (24 mo.)	70	20	40	25	Poor
5	F 45	Preoperative	60	20	60	10	
		Postoperative (23 mo.)	90	30	120	40	Excellent
6*	F 29	Preoperative	60	0	0	0	
		Postoperative (23 mo.)	90	30	120	80	Excellent
7†	M 47	Right, preoperative	20	0	0	0	
		Right, postoperative (22 mo.)	50	10	30	10	Good
		Left, preoperative	30	0	0	0	
		Left, postoperative (22 mo.)	50	10	30	10	Good
8‡	F 37	Right, preoperative	20	0	0	0	
		Right, postoperative (18 mo.)	60	10	70	20	Poor (pain)
		Left, preoperative	30	0	0	0	
		Left, postoperative (19 mo.)	50	10	70	20	Excellent
9	F 30	Preoperative	15	0	0	0	
		Postoperative (19 mo.)	80	20	110	60	Excellent
10	M 59	Right, preoperative	5	0	0	0	
		Right, postoperative (19 mo.)	30	20	0	0	Fair
11§	F 53	Right, preoperative	60	0	0	0	
		Right, postoperative (18 mo.)	75	10	80	20	Excellent
12¶	F 44	Preoperative	65	10	60	0	
		Postoperative (20 mo.)	70	30	80	30	Excellent
13	F 50	Right, preoperative	20	0	20	0	
		Right, postoperative (14 mo.)	60	10	70	20	Excellent
		Left, preoperative	30	0	0	0	
		Left, postoperative (18 mo.)	60	10	70	15	Excellent

*15 degree flexion contracture.
†30 degree flexion contracture each hip.
‡10 degree flexion contracture each hip.
§15 degree flexion contracture.
¶40 degree flexion contracture at left and 5 degrees at right hip.

always guarded by muscle spasm and pain. Arthrotomy was performed under spinal anesthesia. When the femoral head was dislocated it was found that there was an extensive system of periacetabular osteophytes present, but the cartilage was in fair condition, being the least degenerated and worn of any of the cases in this series. The head was trimmed about one-third, capped with a hollow plastic hemisphere, and replaced. The patient's postoperative course was prolonged somewhat requiring her to remain in the hospital for 10 weeks following operation. Convalescence was further complicated by a slight but persistent anemia (hemoglobin 58 to 65 per cent, red blood cells, 2,300,000 to 3,700,000 per cubic millimeter). Diet, hematinic drugs, and transfusions appeared to influence the anemia but little. Convalescence was further prolonged by the patient developing lymphedema of both lower extremities below the knees. This latter was partially controlled by Unna's paste boots. Following the operation, this patient has been able to get about only with the aid of crutches, largely because of the complications noted.

This case is considered a poor result because of the nonorthopedic complications, although a good mechanical result was secured in the hip. This case is also considered a poor selection (age, persistent anemia, muscle weakness, and edema of both lower extremities).

CASE 5. Female, aged 45 years, stated that when she was 9 years of age, she had fallen from a roof injuring her hip. This was followed by a prolonged convalescence. There had always been some pain in the hip from that time (secondary osteoarthritis). Fifteen years prior to operation the pain reached an annoying point and had been gradually progressive during this latter period. Prior to operation she could walk only one or two blocks due to pain and disability of the hip. At operation, a slab of bone 1.5 by 1 centimeter was found in the anterior portion of the capsule. The hip was found to be blocked in abduction by articulating osteophytes on the one side from the head and on the other side from the cervicotrochanteric region. After dislocation, the head was found to be egg-shaped, the large adductor osteophyte being one portion of the mesial projection of the head. The head was reduced to about one-half its former volume, capped with a hollow plastic hemisphere, and replaced. The range of postoperative motion is shown in Table II. The patient has been entirely relieved of pain but continues to have a slight gluteal gait which has been greatly improved by a 0.5 inch lift on the shoe heel of the leg operated upon.

CASE 6. Female, aged 29 years, had had pain and stiffness in the right hip for 12 years prior to operation. On careful questioning the patient stated that "hip joint disease" had been diagnosed at the age of 12 and that roentgenograms has been made of the hip 10 years prior to the time she consulted me at the Guthrie Clinic and the Robert Packer Hospital. These roentgenograms were available for inspection and showed some changes in the hip which were probably those of an ancient slipped upper femoral epiphysis, and secondary osteoarthritis (Figure 11). A large wedge shaped infarct was located in the head. This infarcted area had remained almost unchanged in roentgenograms through the 10 year period. Physical examination showed that the right hip had been converted into a hinge joint (Table II). At operation a large ledge of sclerotic acetabular new bone was found to project anterosuperiorly. A large exostosis from the femoral head articulated with a corresponding structure originating from the trochanteric region, explaining the patient's lack of rotation and abduction. After dislocation of the head, this structure was found to be wedge-shaped, and the relation of the neck to the head was greatly distorted. The head was trimmed to half its former volume, 50 grams of bone being removed. The head was then capped with a plastic cup and replaced. The capsule was loosely reconstructed with interrupted stitches of silk. The patient made a very rapid recovery from the operation and discarded crutches 3 months later. When last seen 13 months following the operation, the range of motion in the diseased hip was practically normal (Fig. 12). The patient complained of no pain and had been extremely active for many months on it.

CASE 7. Male, aged 47 years, stated that 10 years prior to being seen in the Guthrie Clinic and the Robert Packer Hospital he had had an acute attack of multiple arthritis which had left both hips fairly stiff. However, he had been able to get around with little aid except from canes until 1½ years prior to admission. At that time the pain had become so severe and continually disabling that he had remained in bed for 1½ years prior to admission.

Upon examination, both lower extremities were found to be almost fixed in 45 degrees' external rotation and slight flexion (bilateral osteoarthritis, secondary to atrophic arthritis). There was no motion at any plane about the hip except 20 to 30 degrees in flexion. Plastic cup arthroplasties were performed on both hips, 10 days elapsing between operations. The findings in both hips were similar: there was a very fine line of osteophytic bone projecting from the anterior, superior, and inferior portions of the acetabular head. On both sides the femoral head was ovoid in shape. Islands of avascular bone were found in both, in addition to cartilage degeneration. Both femoral heads were reduced about one-half in volume, 50 grams of bone being removed from the left hip and 55 grams from the right. The patient was discharged, walking with crutches 2 months following the last operation. This patient's preoperative and postoperative courses were complicated by obesity which limited his postoperative exercises somewhat. While the patient has been unable to be ambulatory without the aid of crutches during the year succeeding the operation, the range of motion in the hip has been doubled and he has secured motion in abduction and rotation, and he has been converted from a bedridden patient to an ambulatory one. The outlook is that he will continue to need crutches, but there is no evidence of restriction of motion during the year following the operation. He has complained of no pain during the 10 months he has been fully ambulatory following operation.

CASE 8. Female, aged 37 years, stated that she had been in good health prior to 1½ years before admission, when she began to suffer intermittently from pain in both feet, She had suffered intermittently from pain in both knees, both ankles, and both hips during the interval mentioned but during the 1½ years prior to admission her disability was chiefly that present in both hips. Roentgenograms (Fig. 13a) showed osteoarthritis of both hips. Plastic cup arthroplasties were performed on either hip, the operations being spaced at an interval of 3 weeks. Changes found in the hips were similar on the two sides, there being an extremely deep acetabulum present (Figure 13b). Osteophytic new bone had proliferated about the superior and anterior margins of both hips. The dislocated head was trimmed to about one-half its previous volume, most of the bone being removed from the inferior and mesial portions of this structure. Eighty grams of bone were removed from each hip, and the patient was discharged from the hospital 6 weeks following the second operation. During the succeeding 9 months she has maintained the amount of passive and active motion present upon discharge. This patient, however, has complained intermit-

tently of pain in both knees and in the right hip, the former being present to greatest extent during the month following the operation on her hip. The patient also has complained somewhat of "muscle pain" in the right thigh (referred pain). The left hip has been entirely asymptomatic. This patient is considered as completely relieved of pain in the left hip and markedly relieved of pain in the right one. The symptoms in the latter are associated with the progressive collapse of the trimmed head and neck (Fig. 13c). The transparent plastic cup has allowed a correct evaluation of the cause of failure to relieve pain in the right hip.

CASE 9. Female, aged 30 years, was entirely well until the age of 14 years, at which time she was taken by a febrile illness accompanied by acute pain in the right shoulder and left hip. At that time she was confined to bed for 4 months, and no operation was performed on the hip. Roentgenograms made then showed an "infected hip," but these films were not available to us. The patient had suffered so much pain at the left hip that she had been using crutches for 2 years and had markedly restricted her activities 1 year prior to this time (osteoarthritis, secondary to juvenile pyogenic arthritis.) At operation, an extreme anteversion of the head and neck was found. A large line of osteophytic new bone was found inferiorly and anteriorly, and three large size adductor osteophytes were found on the head (Fig. 14). The head was trimmed to one-half its previous volume, and the osteophytes were removed from the head and the neck. The head was capped with a plastic cup and replaced. Total weight of bone removed was 55 grams.

This patient has had an excellent postoperative course, being discharged 30 days following operation. Increase in postoperative motion in her hip has been gradual but progressive especially during the past 6 months. She has been totally relieved from pain.

CASE 10. Male, aged 59 years, stated that he had had attacks of pain in both hips at the age of 14 years, at which time he was living in Gratz, Austria. He stated that he has had some pain and disability in both hips intermittently since that time but both hips have been more painful during the past 10 years. Marked restriction of motion had been noted during the previous 10 years. On admission to the Guthrie Clinic and the Robert Packer Hospital, there was only a slight amount of motion in either hip, both of which were held in about 45 degrees' external rotation.

At operation, extreme difficulty was experienced in dislocating the right hip. This was explained by the complicated and ramifying system of adductor osteophytes. This complicated osteophytic projection was about two-thirds the size of the femoral head, projecting into a similar irregular erosion in the acetabulum. Following dislocation of the hip, this structure was trimmed to one-half its previous volume, capped with a plastic hemisphere, and replaced.

The patient's postoperative course was slow. This patient has never developed motion in the right hip comparable to that in other cases.

This is graded as only a fair result and is now considered to be an error in selection (age, muscle weakness, bilateral extensive involvement).

CASE 11. Female, aged 53 years, had foot pain and disability in both hips 10 years prior to admission to the Guthrie Clinic and the Robert Packer Hospital. During the 5 years previous to admission the left hip had been progressively stiffening and on admission there was a marked flexion deformity in it.

Plastic cup arthroplasties were performed at 4 month intervals. During the interim there had been a "squeak" in the left hip, the site of the first operation. This hip was explored 2 weeks following the second arthroplasty. It was found that a tight scar tissue band had bridged the inferior acetabular notch. The squeak was reproduced and appeared to originate from the band. Section of it abolished the squeak and it has not returned following exploration. Findings in both heads were similar, as an unusually large ledge of exostotic new bone had grown from the superior and anterior margins of the acetabulum (Fig. 15). Islands of avascular bone were found in both femoral heads. Cartilage of both heads was only slightly degenerated but markedly ridged and pleated. The patient was almost totally relieved from pain following operation.

CASE 12. Female, aged 44 years. Disability began in the left hip at the age of 15 years (osteoarthritis of the left hip secondary to slipped upper femoral epiphysis).

Examination of the left hip on admission to the Guthrie Clinic and the Robert Packer Hospital showed 20 degrees' flexion deformity of the left hip and other passive motion as noted in Table II. At operation a large ledge of osteophytic new bone was found anteriorly and superiorly on the acetabulum. There was a large ring of new bone which originated chiefly on the inferior portion of the head and extended around three-fourths the circumference of this structure. The osteophytic new bone was trimmed away, and the volume of the femoral head was reduced to about one-half its previous volume. Cartilage was everywhere thinned, and the weight of new bone removed was 45 grams. This patient had a good postoperative course.

CASE 13. Female, aged 50 years, had been seen on several occasions in the Guthrie Clinic and the Robert Packer Hospital over a period of several years, prior to admission. Plastic cup arthroplasties were performed on both hips at 4 month intervals. The findings in both hips were similar. The lateral surface of the femoral head was relatively inconspicuous due to the structures having sunk into the acetabulum (Fig. 15). There was little evidence of exostotic new bone on the acetabulum except for a moderate amount on the anterior and inferior portions. After both hips were dislocated, extensive cartilage degeneration was identified. Plastic cups were fitted to the femoral head, and these in turn reduced into the acetabulum. The postoperative course was excellent, and the patient had complete relief of pain in both hips.

ANALYSIS OF STUDY

The results in this series of cases have been encouraging. While motion has been restored in most of the cases, such a result is secondary in importance to relief of pain. The end-results of an increase in motion in the hip joint are to some extent dependent upon the amount of motion originally present. It is seldom that more than 45 degrees of passive flexion can be obtained by operation in the average osteoarthritic hip of several years' duration when only a few degrees of motion are present prior to operation. Such cases are usually in the older age groups and, either due to this or other factors, have poor muscula-

ture. An enthusiastic co-operative patient with at least 30 degrees' variation in flexion in the hip prior to operation is the ideal for an end-result in which near normal motion is obtained (see Cases 3, 5, 9, 11, and 12). The objections raised by some that a deeper cup is required to secure the optimum of motion following the operation is not borne out by our results. It is our opinion based upon the exploration of one of our cases and of several others performed elsewhere that when metallic cups have been used, mature fibrous connective tissue is constantly found adherent to the femoral neck and to trochanteric bone. From theoretical consideration the optimum of hemostasis which can be secured only by hot moist packs in this type of operation and a subsequent attempt to reconstruct all or part of the capsule, followed by early and persistent postoperative mobilization, should all favor the optimum of motion. In cases in which subsequent exploration is carried out and in which cartilage was not removed from the acetabulum at the first operation, the presenting portion of this structure was found coated with a layer of scar and fibrocartilage. This would tend to show that removal of cartilage from the interior of the acetabulum is not necessary in this condition unless the interior is so malformed that a loose fit is not obtained when the capped femoral head is replaced. In 2 cases in our series (Cases 2 and 4), a good mechanical result was obtained, but the patient was not substantially benefited, in 1 case because of muscle weakness and lymphedema, while multiple arthritis hampered his activity in the other case.

In general, there has been little increase in active or passive motion in the months following discharge from the hospital. Motion has decreased in those patients who have had little preoperative motion and who have been unwilling to continue vigorous exercise. A slight increase of 10 to 30 degrees in all planes has been observed in the first year in those vigorous patients with excellent postoperative results.

Relief from pain has been complete in about half of our cases. Again, this evaluation has been approached critically. Total relief has been obtained in two classes of end-results: those with muscular vigor and a fair postoperative range of motion and those who have obtained only a moderate increase in motion following the operation. If even slight "muscle pain" has been present following the operation, either on change of weather or excessive use of the extremity, then subtotal relief of pain has been recorded for that patient. The estimation of the degree of relief from pain is difficult to make, but from a careful consideration of the patients' statements and their ability to use the hip operated upon, relief is approximated at about 90 per cent in those in which relief from pain was not complete. So far as the author is concerned, the only operative procedure applicable to patients with osteoarthritis following which relief from pain is complete and definitely predictable is arthrodesis of the involved joint. However, this is not possible nor desirable in many patients.

It is our impression that the relief from pain is definitely greater with the use of the plastic cap (molded from sheet material) than is obtained following metallic cup arthroplasty in patients suffering from osteoarthritis. Surface hardness of the interposed material probably is the responsible factor, since relief from pain was far less in 3 patients upon whom we have performed an arthroplasty with a pure fused quartz cup than in those in which the plastic cup was used.

Fluoroscopic studies have been made at intervals on 6 hip joints in which the plastic cup was fitted with a rim of stainless steel (Figs. 14b and 15b) embedded in the cup margins. These observations show that motion is preserved at both interfaces of the cup, but as time progresses (more than 2 months after the operation) the motion of the femoral head within the cup is the predominating one. Motion between the cup and acetabulum is observed in these latter months to occur with regularity only in the extremes of rotation, abduction, and adduction. It is our impression that the best mechanical result is obtained when this biplanar motion is preserved and the transition or shift from one to the other occurs smoothly. A poorly fitting cup (in either plane) will restrict motion in one or the other plane, and if it binds, the patient has the sensation of a locking or snapping joint.

Another advantage of the plastic cup is its transparency to the roentgen ray. So far, in the observation of these patients and of others in which operation was performed for other conditions, changes have been observed in the head-neck stump within the cup in but 2 cases. A portion of necrotic bone apparently 3 millimeters in diameter, from an infarcted area in the head became loosened and dropped into the dependent portion of the joint (Fig. 10c) but has caused no trouble. In another case (Fig. 13c), the mesial portion of the head has flattened under weight bearing. This has been coincident with loss of abduction and pain in the leg. However, insufficient time has elapsed entirely to cover the period during which changes

are likely to occur. Collapse of the head and neck has occurred in only 1. It should be pointed out that the circulation through the ligamentum teres vessels is nonexistent even prior to operation in most osteoarthritic hips.

It is the opinion of the author that foreign body molds should be left in place indefinitely so long as they do not give rise to symptoms. We have not found it necessary to remove any from our cases because of infection or because of other untoward effects. A limited experience based upon the exploration of hips following metallic cup arthroplasty indicates that thickness of fibrocartilage formed is not such as would long withstand the trauma of weight bearing.

ARTHROPLASTY IN OTHER JOINTS UTILIZING PLASTIC CUPS

We have had the opportunity to perform arthroplasty upon the metacarpophalangeal joints and upon the temporomandibular joint utilizing smaller cups (9, 11, and 13 millimeters) of methacrylate plastic. The results in all cases were excellent. In the finger joints mentioned, relief from pain was complete and there was restoration of motion due to this factor. In this joint (Burman) it was necessary to cut away and reshape the distal metacarpal head prior to fitting the plastic cup to it, since in this instance the cup is used to cover the distal metacarpal head, the proximal phalanyx being left untouched. The roentgenograms of Figure 16 show the restoration of "joint space" in a patient with quiescent atrophic arthritis presenting marked pain associated with almost complete cartilage destruction. The mechanical result obtained at the temporomandibular joint (previously totally ankylosed in bone) was excellent, but insufficient time has elapsed to evaluate this result fully. The indications for the use of these smaller cups at the metacarpophalangeal joint appear to be pain, associated with cartilage destruction when the arthritic process is quiescent.

SUMMARY

Late results, approximately 18 months following foreign body cup arthroplasty of the hip in osteoarthritis utilizing a plastic methacrylate cup (lucite, plexiglas, etc.) are reported in 13 cases (16 hips). The results have been "excellent" in 10 hips, or 62.5 per cent, "good" in 3 hips or 18.7 per cent, and "poor" in 3 hips or 18.7 per cent. Viewed in retrospect, 2 of the latter cases were errors in selection since a good mechanical result obtained in these patients had to be rated as "poor" due to the inability of the patient to utilize the result due to systemic causes. In the third, pain was associated with the collapse of the neck fragment (Fig. 13c). Osteoarthritis of the hip is a degenerative phenomenon involving primarily the joint cartilage and perhaps the underlying bone. Secondary changes of osteophytic proliferation and further sclerosis and enlargement of the head then occur. In our series, 37 cases, or 39.4 per cent, demonstrated some primary hip joint disease which was succeeded many years later by the typical alterations of secondary osteoarthritis. The anatomy of the hip and the gross and microscopic changes in osteoarthritis are described.

Plastic cups are totally transparent to the roentgen ray, so that osseous changes occurring in the hips can be visualized. The material appears to be well tolerated, its further use appears to be warranted, in this and other conditions in which hip joint arthroplasty is indicated. More time and experience will be required to determine if less pain is experienced by the patient with osteoarthritis upon whom a plastic cup arthroplasty is performed as compared with the use of metallic cups. Present experience points to the affirmative.

A simplified operative technique is described which is applicable in the presence of a movable hip. According to this modification, it is necessary to reshape only the femoral head when a suitable fit is already present between the exterior of the cap and the acetabulum, and the amount of muscle detachment from the ilium is reduced to a minimum. It is recommended that the hip joint capsule be closed with interrupted stitches of suitable material.

Smaller cups of the same material are applicable in arthroplasty of the temporomandibular joint and in the metacarpophalangeal joint.

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PLASMA CLOT AND SILK SUTURE OF NERVES

I. An Experimental Study of Comparative Tissue Reaction

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THE use of silk sutures for the purpose of maintaining the ends of a severed nerve in apposition and thereby facilitating growth of the regenerating neurofibrils is not always an entirely satisfactory procedure. This is particularly true in the case of small nerves in which the silk ties are apt to strangulate a considerable proportion of the nerve fibers while the almost unavoidable distortion at the site of junction offers additional interference with regeneration. Young and Medawar have sought to avoid these difficulties by employing clotted plasma instead of silk to keep the nerve ends in correct alinement. They considered mammalian plasma unsuitable for this purpose and confined their efforts to the use of cockerel plasma. In experiments in which the sciatic nerves of rabbits were sutured by this method, the clots proved to have insufficient holding power. These investigators, however, found that they could improve the tensile strength of the clots by fortifying the plasma immediately before use with several times its normal content of cockerel fibrinogen. With clots prepared in this manner, they obtained encouraging results.

Our studies (3) began with attempts to repeat the experiments of Young and Medawar. Suture of the sciatic nerve in rabbits was carried out with the use of fortified cockerel plasma clotted by the addition of chick embryo extract. However, histological examination of the suture site made at varying periods after operation disclosed the presence of considerable inflammatory and fibrotic reaction. Since a cicatricial reaction may seriously hamper regeneration of nerve fibers, our experiments were directed to the study of plasma clots which would provoke minimal tissue reaction but would nevertheless possess sufficient strength and adhesive properties for successful suturing. It developed that mammalian and more particularly, autologous, plasma was superior to cockerel plasma since it was unnecessary to augment the fibrin content of the mammalian clot and less inflammatory reaction occurred in and about the sutured nerves. The present communication describes the character and extent of these tissue reactions and records the measures we have adopted to obtain a secure junction of the nerve ends.

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PROCEDURE

Adult male and female rabbits were used in most of the experiments. Nembutal was employed as the anesthetic in the first 5 animals but ether was used subsequently. Greater relaxation of tissues with less retraction of the severed nerve ends occurred when the animals were under ether anesthesia. A muscle splitting incision through the buttock was made following which the sciatic nerve was exposed, freed, and cut approximately 2 centimeters distal to its exit from the pelvis. In the first 9 animals the nerve was cut with a scissors; in the subsequent operations a sharp razor was used. After the nerve was cut, retraction of the ends for a distance of 1 to 2 centimeters was usually observed. The slight amount of bleeding from the cut ends was easily controlled by means of gentle pressure with cotton pledgets soaked in warm saline solution. Before the suture was performed, the limb was so placed that the nerve lay in a horizontal plane. This position minimized the tendency of the plasma to run off from the suture site before it had clotted around the nerve junction.

The cockerel plasma was prepared according to the technique described by Young and Medawar. Both unfortified and fortified (6 times normal concentration) plasma were used. Coagulation of the plasma was effected by the use of chick embryo extract as recommended by these authors.

Blood from rabbits was obtained under aseptic conditions by cardiac puncture, that from human subjects by venipuncture in the usual manner. In a few of the early experiments 1 cubic centimeter of 3 per cent sodium citrate was added to 9 cubic centimeters of rabbit or human blood to prevent spontaneous clotting. To promote clotting 1 drop of 1 per cent calcium chloride was added to 0.25 cubic centimeter of the citrated plasma before the addition of the tissue extract. In subsequent experiments, either heparinized or unmodified blood was used as the source of plasma. The heparinized blood was collected by

withdrawing 9.5 cubic centimeters of blood into a syringe containing 0.5 cubic centimeter of a 1:100 dilution of heparin. In order to prevent clotting of the unmodified blood the syringe, previously chilled, was coated with mineral oil and the blood immediately transferred to paraffin-lined test tubes packed in ice. The blood was centrifuged for 5 to 7 minutes at 2750 revolutions per minute in large metal cups filled with ice.

In some of the early experiments lung extract was used to promote clotting of the plasma. The lungs of a small mouse were removed aseptically, washed with a small amount of physiological saline solution, minced, and then ground in a mortar with the addition of 10 drops of normal saline solution. The suspension was then centrifuged and the clear supernatant fluid used as the clotting agent. It was thought that autologous tissue extract as the clotting agent might lessen the local postoperative reaction, and muscle was investigated for this purpose. Although muscle extract was not as efficacious as lung extract in inducing rapid clotting, satisfactory results were obtained when the muscle extract was prepared in a specially concentrated form. The tissue was removed from the gluteal region about 2 centimeters above the site of the proposed nerve suture and the precaution was taken to keep the traumatized area separated from the sciatic nerve by intact muscle. A piece of muscle weighing about 2 grams was excised, minced, and ground in a mortar with sand and 7 to 10 drops of normal saline solution. The suspension was revolved at maximum speed in an angle centrifuge and the supernatant fluid was then removed by pipette.

The technique of performing the nerve suture in rabbits consisted in bringing the retracted stumps together by means of fine jeweler's forceps, depressing the junction into the fascial and muscle bed so as to form a trough, and adding first 5 drops of plasma and then 1 drop of tissue extract. The fluids were thoroughly mixed *in situ* and then about 2 to 3 drops of the mixture were withdrawn into a pipette to reduce to a minimum the amount of clot remaining as suture material. Although clotting occurred in about 40 seconds the nerve ends were held together with the forceps for about 4 minutes to make certain that the clotting process was complete. After release of the forceps, separation at the suture site frequently occurred. Usually the clot was removed after such separation and the procedure was repeated.

Silk suture of the sciatic nerve was done in some cases for the purpose of comparing the resultant tissue reaction with that which followed plasma clot suture. The technique of the silk suture consisted in using 2 silk stitches on opposite sides of the junction. Each suture consisted of 1 of the 3 component strands obtained by unravelling fine number 4 silk. An attempt was made to confine each stitch, so far as possible, to the nerve sheaths.

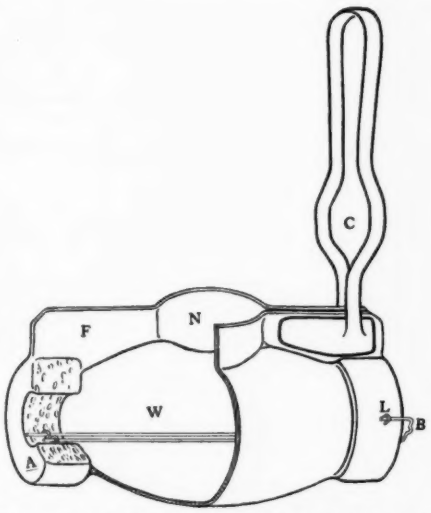


Fig. 1. Sketch of latex mold used for plasma clot suture of nerves. *W* represents wire supporting rails which prevent sagging of the nerve ends. The rails (No. 34 nickel silver), which are removable, are threaded through wire loops in the base of the air-foam collar, *A*. The handle, *B*, of each rail is held in place by a wire loop, *L*. Metal clips, *C*, are applied to the fins, *F*, of the mold. The clips serve to tighten the grip of the air-foam collars and thus prevent retraction of the nerve as well as leakage of plasma. Plasma is introduced into the mold through the funnel, *N*.

Usually both sciatic nerves were cut and different suture material was used on the two sides. In a few instances the nerve was cut, and the ends were held together for 4 minutes as for clot suture but were not actually sutured. In a few other instances, nerve suture was attempted with whole blood. Closure of the wound was carried out in a uniform manner in all cases. Interrupted fine silk sutures were used in the fascia covering the muscle and the skin edges were approximated with continuous fine silk sutures.

More recent experiments have been carried out in dogs. The experiences gained from the operations in rabbits made it clear that the surgical technique employed in these animals was inadequate. One of the most serious difficulties lay in the fact that the procedure of holding the nerve ends in apposition at the base of a trough formed by the neighboring tissues permitted the added

TABLE I.—INCIDENCE OF SEPARATION AND DEGREE OF HISTOLOGICAL REACTION ASSOCIATED WITH VARIOUS TYPES OF NERVE SUTURE IN RABBITS

Type of suture	No. of operations	No. of operations in which separation of nerve ends was observed following suture		Intensity of tissue reaction showing number in each group*			
		Immediately at operation	Later at autopsy	+	++	+++	++++
Rabbit plasma clot Unmodified	5			5			
Heparinized	10	2	2	7	3		
Citrated	4	2	1	3	1		
Total	19	4	3	15	4		
Human plasma clot Unmodified	5	1		1	4		
Heparinized	7	2	2	1	4	2	
Citrated	1	1			1		
Total	13	4	2	2	9	2	
Cockerel plasma clot† Fortified	8	3	2		1	2	5
Unfortified	1	1		1			
Total	9	4	2	1	1	2	5
Whole blood	2	2	1	1	1		
Silk	6			2	4		
Nerve cut but not sutured	3	3		3			

* 4 plus represents maximal and 1 plus minimal intensity of inflammatory and fibrotic response. †Cockerel series includes 1 capon.

plasma to coat only one side of the nerve junction. To overcome this objection the technique was modified in the experiments in dogs. In these animals suture of the nerve was carried out in a rubber mold designed to retain the plasma at the suture site so as to produce a clot completely and uniformly surrounding the nerve junction.

The mold which was used in our early operations in dogs was made of latex in the form of a hollow tube wide open along its entire length and with a cup shaped depression in the center. Its chief fault lay in the fact that it did not provide for adequate coating of the superior surface of the nerve. After the central cup was filled, any additional plasma tended to escape from the ends of the mold. A spherical latex mold with sleeves attached to envelop the nerve ends was used in subsequent operations. An opening was cut in the top of the mold to permit manipulation of the nerve stumps and introduction of the plasma. A slit extending from the opening to the ends of the sleeves was made to allow for the application and removal of the mold. Leakage of plasma at the sleeve ends still occurred occasionally since the size of the nerves which were sutured varied. A number of modifications of the spherical mold were made. A sketch of the mold[1] which was used in a few of the more recent operations, the results of which are included in this report, is shown in Figure 1.

The technique in other respects was essentially similar to that employed in the operations on the rabbits except that nembutal was used as the anesthetic, the nerve was cut with a sharp scalpel and silk sutures of nerves were performed with the use of 4 rather than 2 stitches. After the nerve was cut, less retraction of the stumps occurred in the dog than in the rabbit. Seven to 15 drops of homologous or autologous plasma were used and clotting was either allowed to occur spontaneously or was induced by addition of autologous muscle extract or rabbit clotting globulin. After complete clotting had occurred, the rubber mold was carefully peeled away and removed. As in the case of the rabbits, no attempt was made to immobilize the limb after operation.

Specimens of nerve were obtained at the time of autopsy or second operation 4 days to 185 days after the nerve was sutured. The tissue was fixed in 10 per cent formalin. The portion of nerve at the suture site was embedded in paraffin and stained with hematoxylin and eosin as well as by the Bodian technique for demonstrating nerve fibers. In a few instances the segment at the nerve junction was cut on the freezing microtome and the sections were treated with silver

[1] The molds which we have used were made by Mr. Saul Swarz, Secretary of the Clay Club of New York, and Mr. Cornelius Denslow. A complete description will appear in a later publication.

TABLE II.—INCIDENCE OF SEPARATION AND DEGREE OF HISTOLOGICAL REACTION ASSOCIATED WITH VARIOUS TYPES OF NERVE SUTURE IN DOGS

Type of suture	No. of operations	Number of operations in which separation of nerve ends was observed following suture*	Intensity of tissue reaction showing number in each group			
			+	++	+++	++++
Unmodified dog plasma† without clotting agent‡	16	5	8	4	2	
Unmodified dog plasma with rabbit clotting globulin	7	3	4	2	1	
Unmodified dog plasma with autologous muscle extract	5	1	2	2	1	
Heparinized dog plasma with rabbit clotting globulin	13	4	7	5		
Heparinized dog plasma with autologous muscle extract	3	0	2	1		
Whole blood	2	2		2		
Silk	11	0	8	3		
Nerve cut but not sutured	1	1	1			

*Separation of nerve ends was observed at autopsy in each instance rather than immediately after suture at operation.
†Homologous plasma was used in 2 instances in which the intensity of tissue reaction was 1 plus and 2 plus; in the remaining experiments with clot suture, autologous plasma was used.
‡2 animals in this group and 1 in which heparinized plasma with rabbit clotting globulin was used were not studied histologically.

nitrate according to the Gros-Bielschowsky technique for impregnating axis cylinders. Segments of the nerve distal to the suture site were cut and Gros-Bielschowsky and Weigert-Pal preparations for the staining of axis cylinders and myelin sheaths were made.

Measurements of tensile strength of clots prepared from many samples of rabbit, dog, and human plasma were carried out. The values were obtained by an improvised method which proved simple and, in its final form, gave fairly consistent results (4). A detailed report of these studies will appear in a separate communication (1).

RESULTS

Of 41 instances in which all types of plasma clot suture were performed in rabbits, immediate and complete separation of the stumps to the extent of 1 millimeter or more occurred in 13, or almost one-third, of the total number (Table 1). In 8 of these instances the separation exceeded 2 millimeters. There were 6 additional cases in which good apposition of nerve ends was present at the time of operation but in which subsequent examination of the suture site at autopsy revealed complete separation of the stumps. The total number of operations in which early or late separation occurred was 19, an incidence of about 46 per cent. The highest incidence of separation occurred in those cases in which suture was performed with the use of cockerel plasma clot. It should be noted that cockerel plasma clots differed strikingly from clots prepared from human, dog, or rabbit plasma in being relatively nonretractile, inelastic, and friable.

In the operations on dogs separation of nerve stumps occurred in 13 of 44 instances, or 29.5 per cent of the attempted sutures which included a variety of types of plasma clot (Table II). Reduction in the incidence of separations was attributable to improvements in technique resulting largely from the use of the suturing mold.

The intensity of the tissue reaction at the suture site was evaluated after comparative study of histological sections of the nerve junction obtained at variable periods after operation. The reactions, ranging from 1 plus to 4 plus have been recorded in Tables I and II.

In the dog and rabbit the tissue reaction at the suture site was often very slight. In many instances the reaction was characterized by the appearance of a few connective tissue fibers and an occasional thin walled blood vessel, lymphocyte, monocytic cell, plasma cell, polymorphonuclear leucocyte, and fibroblast. Microscopic examination of the nerve several days after suturing with plasma clot revealed a small amount of granulation tissue at the suture site (Fig. 2), with homogeneous or granular eosinophilic material which represented the residual fibrin of the plasma clot. Lipophages were sometimes present in moderate numbers at this stage. Weeks later almost no signs of inflammatory reaction with the exception of a minimal increase of fibroblasts and connective tissue were observed at the nerve junction (Figs. 3, 4, and 5). In some instances in

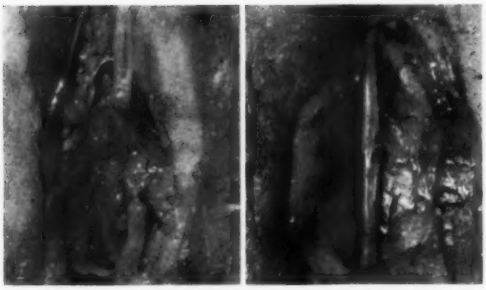


Fig. 2. a, left, Cut sciatic nerve of a dog which was unsutured. Note degree of retraction of stumps present 5 days after operation. b, right above, Opposite sciatic nerve of same dog which was sutured with 8 drops of autologous heparinized plasma mixed with 1 drop of rabbit clotting globulin. Specimen was obtained 5 days after operation. c, right, Section through suture site of nerve shown in b. Note the small amount of granulation tissue present at the suture site. Hematoxylineosin stain. × 26.

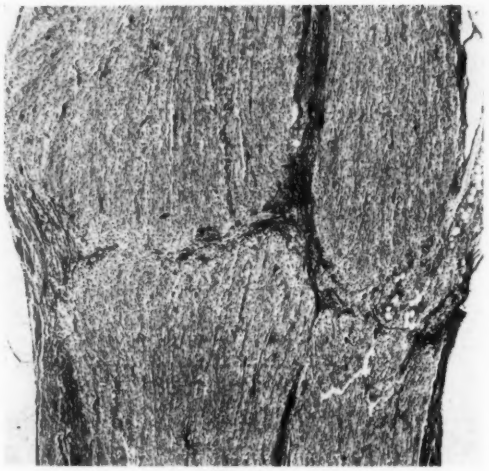
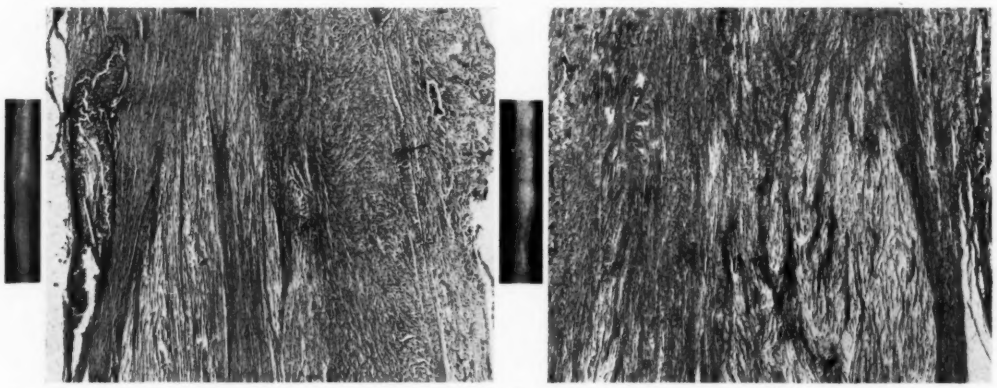


Fig. 2c.

which silk was used for suture, the only evidence of tissue reaction was encapsulation of the silk fibers by connective tissue (Figs. 3a and 8b). Such reactions were graded as of 1 plus (1+) intensity in the tables. They were characteristic of the tissue response when silk or autologous or homologous plasma was employed as suture material. Less commonly they occurred after the use of heterologous plasma. It may be added that in those instances in which separation of nerve stumps occurred, granulation tissue tended to be more abundant than it was when the nerves were successfully sutured.

The most intense inflammatory reaction and fibrosis (++++ in tables) at the suture site was found in the animals in which cockerel plasma and chick embryo extract were employed (Fig. 6). Diffuse and focal accumulations of large numbers of polymorphonuclear leucocytes, monocytic cells, lymphocytes, plasma cells, and occasional multinucleated giant cells were regularly noted. The inflammatory cells were usually scattered throughout the region of the nerve junction. Numerous thin walled blood vessels, connective tissue fibers, and fibroblasts were also present in this area. As the intensity of the inflammatory



a b c d

Fig. 3. a, Photograph of dog's sciatic nerve sutured with silk 86 days before death of animal. b, Section through suture site of nerve shown in a. Note the encapsulated silk on the left. c, Photograph of opposite sciatic nerve of same dog sutured with 8 drops of autologous unmodified plasma. d, Section through suture site of nerve in c. Little evidence of inflammatory or fibrotic change. Specimen obtained 86 days after operation. Hematoxylineosin stain. × 28.5.

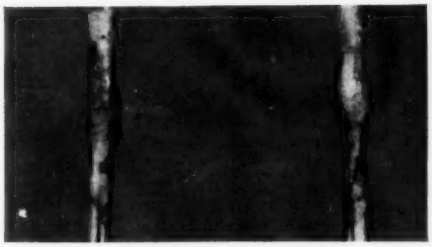


Fig. 4. a, above, Photographs of a dog's sciatic nerves sutured with autologous unmodified plasma 35 days before specimens were obtained. Nerve on left was sutured with 11 drops of plasma mixed with 1 drop of rabbit clotting globulin, that on right with 8 drops of plasma and 1 drop of autologous muscle extract. b, Section through suture site of nerve shown on left in a. Suture site, indicated by arrow, is almost invisible. Hematoxylineosin stain. × 25.

Fig. 4b.

reaction subsided an increase of collagen and reticulum at the suture site became apparent.

The tissue reactions of intermediate grade (++ and +++) consisted of lesser focal accumulations of monocytic cells and lymphocytes (Fig. 7a). At times polymorphonuclear cells with multinucleated giant cells, plasma cells, thin walled blood vessels, fibroblasts (Fig. 8a), and connective tissue fibers were present in moderate numbers. These intermediate reactions usually occurred when heterologous plasma (human or cockerel) was used although occasionally they also followed the use of autologous plasma clot or silk suture (Fig. 8a).

In general it may be stated that less cellular reaction occurred when autologous rather than heterologous plasma was used (Fig. 9, a and b). However, no appreciable differences in cellular response were found following autologous as contrasted with homologous plasma clot suture. At times less inflammatory changes followed suture with plasma clot than with silk but these differences were not consistent. It is uncertain also whether the use of different clotting agents such as mouse lung or rabbit muscle extracts or rabbit globulin caused any added tissue reaction above that resulting from the use of spontaneously clotted plasma.

In those instances in which whole blood was used as the suture material, granulation tissue composed of thin walled blood vessels with an

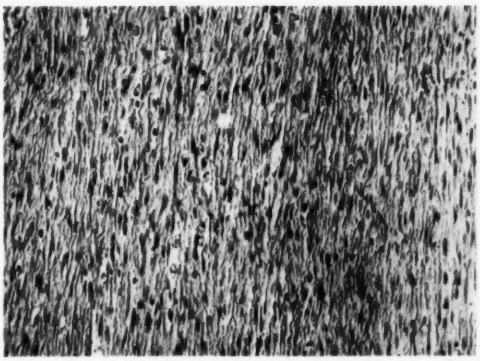
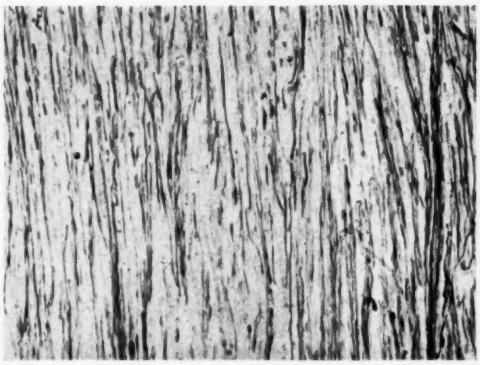


Fig. 5. a, left, Higher power view of suture site shown in Figure 4, b. Note the almost complete absence of inflammatory or fibrotic reaction. Hematoxylineosin stain.



× 133. b, right, Axis cylinders at suture site which have grown through the junction. Impregnation with silver nitrate, Gros-Bielschowsky method. × 118.

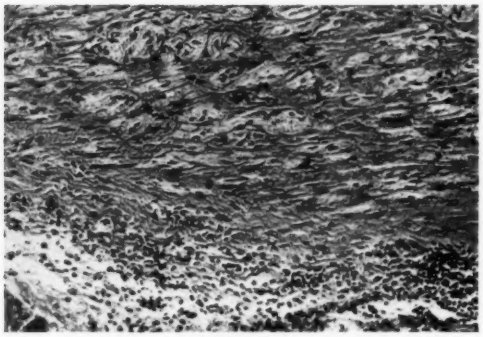


Fig. 6a.

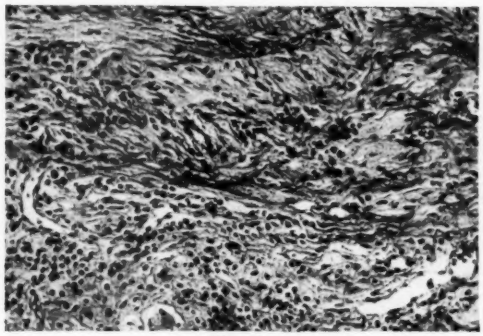


Fig. 6b.

Fig. 6. a, left, Focus of round cells 48 hours after suture with cockerel plasma and chick embryo extract. b, above, Diffuse cellular infiltration 23 days after suture with cockerel plasma without clotting agent. × 133.

occasional lymphocyte, plasma cell, monocytic cell, and polymorphonuclear leucocyte was present. Great numbers of pigment-laden macrophages were found in these cases and, after the lapse of weeks, fibrosis was rather prominent. Separation of the nerve stumps occurred in the few instances in which suture with blood was attempted.

The degree of adhesions which was found grossly between the suture site and the surrounding tissue closely paralleled the intensity of the inflammatory and fibrotic tissue reaction observed microscopically. Only a few delicate adhesions were seen when minimal histological reaction was present. Trauma to the muscle or other tissue adjacent to the nerve as well as hemorrhage during the operation tended to increase adhesions.

Nerve fibers readily grew through the plasma clot junction (Fig. 5b). In Figure 9c myelinated nerve fibers are seen 10 centimeters distal to the suture site. There is at present no indication from these studies that the regeneration of axis cylinders occurs less rapidly after plasma clot than after silk suture. Histological study of the pattern of regenerating nerve fibers following different suturing procedures indicated that less distortion of nerve fibers occurred when plasma clot suture was carried out with the aid of the mold. In contrast with this one may note the greater disorganization of nerve pattern resulting from the use of silk sutures (Fig. 3a).

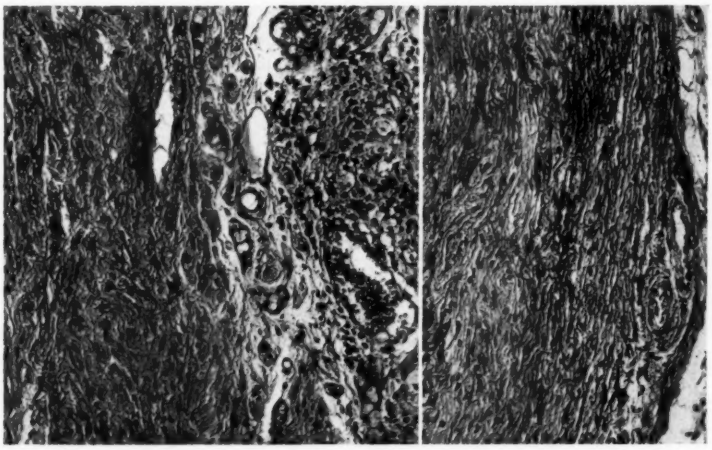


Fig. 7. a, left, Focus of round cell infiltration 97 days after suture with human unmodified plasma. b, right, Minimal histological reaction 59 days after suture with human plasma. × 128.5.

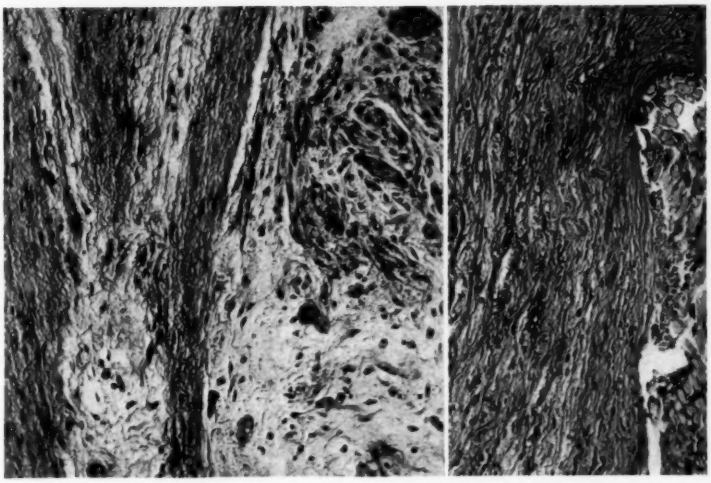
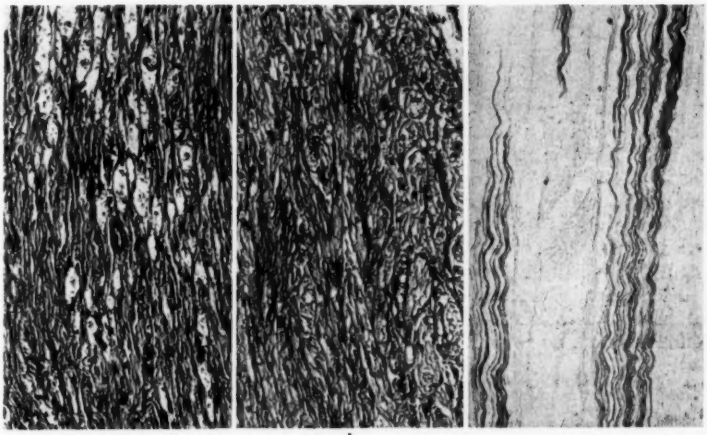


Fig. 8. Photomicrographs showing tissue reaction 28 days, a, left, and 48 days, b, right, after silk suture. Note the foreign body giant cells in a and the connective tissue encapsulation of the silk in b. × 128.5.

EVALUATION

In order to qualify as desirable nerve suture material, plasma clots must not provoke excessive inflammatory or fibrotic reaction of tissues. They must, moreover, possess sufficient strength to maintain nerve ends in good apposition until union by fibroblasts or Schwann cells occurs. Clots formed from 7 to 15 drops of autologous or homologous plasma appear usually to fulfill the first requirement. Under the conditions of the



a b c

Fig. 9. Photomicrographs showing minimal histological reactions at suture site; a, 29 days after autologous unmodified plasma and b, 59 days after autologous heparinized plasma clot suture. × 136. In c nerve fibers are shown stained by Weigert-Pal technique in portion of nerve 10 centimeters distal to suture site; specimen obtained 95 days after autologous unmodified plasma clot suture. × 68. All sections seen in Figures 6, 7, 8 and 9, (except Fig. 9c which is stained by the Weigert-Pal technique) represent suture sites on sciatic nerves of rabbits stained with hematoxylineosin.

experiments as carried out in the present study, the clots failed to meet the second requirement in a high proportion of instances. However, it must be remembered that no form of immobilization of the limbs was attempted following operation. In more recent experiments, following plasma clot suture of the sciatic nerve, the hind limbs have been immobilized by means of plaster-of-paris casts in such a position as to remove tension from the suture site. Conditions are thus rendered more favorable for plasma clot suture. When tension exists at the suture site, plasma clot suture is contraindicated since the risk of separation of nerve stumps is too great.

It must be emphasized that trauma to the nerve ends during their manipulation as well as injury to muscle or other tissues around the nerve or hemorrhage in the region of the suture site all tend to aggravate the inflammatory response of the tissues. Misinterpretations may thus arise as to the amount of reaction attributable to the presence of the plasma clot. It is probable that the histological reaction observed in association with some of the various types of suture material, especially in our earlier operations in rabbits, was due in part to such trauma or hemorrhage. However, special care was taken to avoid such pitfalls in later operations and it seems fair to conclude that the different histological reactions which occurred following the use of various suture materials resulted principally from the substances mentioned.

The greater intensity of the inflammatory reaction around nerve junctions sutured with cockerel plasma as compared with those in which human plasma was used is apparently, at least in part, attributable to the fact that fortified cockerel plasma was used. In the one case in which unfortified cockerel plasma was used, a minimal amount of reaction occurred. It is possible too that the chick embryo extract played a rôle in this greater inflammatory response. That this extract is not the most important factor, however, is indicated by the intense inflammatory reaction which occurred in the 2 instances of cockerel plasma clot suture in which no tissue extract was used.

It is as yet uncertain whether autologous plasma and clotting agents cause less tissue reaction than homologous ones. The observation that less inflammatory change generally followed the use of autologous rather than heterologous plasma is in keeping with the results of Loeb's investigations of blood clots.

It seems clear that the use of the mold makes for a more satisfactory nerve suture. Its advantages lie in the fact that it enables one to secure more perfect alinement of the nerve stumps, it minimizes trauma to the nerve from excessive manipulation and it permits the clot to surround the nerve junction more completely, thereby increasing the strength of the union.

CONCLUSIONS

1. Cockerel or human plasma clot suture of nerves in rabbits generally result in more inflammatory and fibrotic reaction than does silk suture.
2. Autologous plasma clot suture of nerves in rabbits and dogs usually results in very little inflammatory or fibrotic change and compares very favorably in this respect with silk suture.
3. Separation at the suture site frequently follows plasma clot suture in rabbits when small quantities of plasma are used. The incidence of separation was appreciably reduced in operations on dogs by the use of a special rubber mold which retains the plasma uniformly around the suture site during the clotting process.
4. Nerve fibers readily grow through the junction formed by means of plasma clots.
5. Plasma clot suture offers promise as a method of securing junction of nerve ends with minimal distortion of nerve pattern in instances in which the factor of tension at the suture site can be eliminated.

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EDITORIALS

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MARCH, 1943

CANCER OF THE STOMACH

WHILE remarkable results are being obtained in the treatment of cancer of the colon and rectum, cancer of the stomach is far less often cured, and the consequence is that most laymen and many physicians look upon it as a rather hopeless disease. Some of this pessimistic attitude seems to be justified, for even the best reports of treatment of gastric cancer do not compare favorably with those of cancer elsewhere in the body. Since this is so, it behooves the physician and surgeon to try to improve their results. How may this best be done, and what is being done about it?

With improvements in preoperative preparation, technique, equipment, anesthetic methods, and postoperative care, surgeons have greatly widened the field of operability and the extent of operative removable in cases of cancer of the stomach. Total removal of the stomach, which was regarded as a rarity only a few short years ago, is now a more or less standard procedure, and every large clinic in which much gastric surgery is done has its own series of total gastrectomies. While the results of total gastrectomy have not been too brilliant, the aggregate of patients who have lived for one to several years after such an extensive procedure in reasonably comfortable condition must be considerable. For example, from the Massachusetts General Hospital alone in 1938, Arthur Allen[1] reported 16 cases of total gastrectomy, 8 of which "left the hospital in a comfortable state of health." In addition, in nearly every large clinic, surgeons have increased the number of patients operated upon by enlarging their criteria of operability. For example, at the Cincinnati General Hospital in the years 1932–1936 inclusive, 42 per cent of the patients in whom cancer of the stomach was diagnosed were operated upon, the others being deemed inoperable, and in only 9 per cent of these were resections done. In the years 1937–1939 inclusive, 50 per cent of the patients with gastric cancer were operated upon, and in 43 per cent of these resections were done. The same sort of experience has been noted in other hospitals.

The increase in percentage of operable cases is in part due to earlier diagnosis and treatment, but in even greater part to a willingness on the part of surgeons to perform resections in patients who previously would have been regarded as inoperable. One cannot, of course, expect excellent end-results when many borderline cases are treated by resection, but often some months or years of reasonably comfortable life are given to patients who otherwise have a miserable outlook. With increases in the operability, the surgeon has added wider extent of resection to the cases which he regards

[1] Am. J. Surg., 1938, 39: 35.

as favorable. The removal of the great omentum and all of the gastrocolic ligament, excision of the pylorus and the retropyloric glands, the highest possible division of the gastrohepatic ligament with its lymphatic glands, are now recognized to be as necessary as is a wide margin of normal gastric wall beyond the cancer. The work of Earle B. Kay[1] of Ann Arbor has given a scientific rationale for this procedure.

The American College of Surgeons has announced in 1941 a total of 1,279 cases of 5 year cures of cancer of the stomach registered in its Archives of Five Year Cures of Cancer. Undoubtedly there are many more which have been cured but not registered. Nevertheless, the curability of cancer of the stomach still remains comparatively low. The excellent results reported by Waltman Walters,[2] which seem to be the best reported to date show less than 35 per cent 5 year cures. Since it seems unlikely that significant advances in operability or extent of operative resection can be expected it appears that the only ways in which better results can be obtained are for new methods of treatment to be developed or for patients with cancer of the stomach to come to the surgeon earlier. The results of treatment with radiation in cases of cancer of the intestinal tract have been notoriously poor, so that many doctors have eliminated radiation as a form of therapy. This does not mean that at some time in the future, radiation, perhaps by some new technique, may not be an aid in the treatment of cancer of the stomach. At the present time, however, the sole therapy which is of any proven value is surgical removal. There remains then, as a means of improving the cures in this dread disease, the development and use of new ways to establish the diagnosis earlier than has been done in the past, or to discover the cause or causes of the disease and attempt to eradicate them. Along the lines of earlier diagnosis some progress is being made. More accurate and careful roentgenologic examinations, together with increasing numbers of examinations, have been of great help. The introduction of the flexible gastroscope by Schindler and its extended use has been of even greater help. As a supplemental or complemental method to roentgen examination, it is of great assistance and at times superior to the older method. However, the most important factor in earlier diagnosis still is in the hands of the patient himself and the first doctor who sees him. First, the patient must realize that there is something wrong, and, second, when he consults a physician, the latter must be "on his toes" to recognize the possibility of serious disease, and begin a careful and accurate study. Too often, the doctor is worried about the possibility of a fruitless search, yet many such searches may be well repaid, by obtaining one early case that may be cured by prompt surgical intervention. It would not be profitable here to review the early signs and symptoms of cancer of the stomach, or the means to be used to make the diagnosis. They are easily accessible elsewhere.

Regarding the discovery of causes of cancer of the stomach and efforts to eliminate predisposing factors, preliminary studies are in progress. Work is being done at a number of clinics throughout the country, encouraged and partly supported by the National Cancer Institute of the U. S. Public Health Service. The studies that are at present being carried out have to do with careful examination of excised tumors, histologically and chemically, studies on the altered secretory activities of the stomach with cancer, an evaluation of the relationship between atrophic gastritis and cancer of the stomach, the rôle of vitamins in

[1] Ann. Surg., 1941, 113: 1059.
[2] Tr. West. Surg. Ass., 1940, p. 220.

the causation of gastritis and cancer, the possibility of development in the body itself of carcinogenic agents which in turn cause cancer, and the experimental production of cancer of the stomach in animals. These are a few of the projects under way, one or another of which may turn out to be of value. In the meantime, until new methods of treatment are evolved or until a cause for cancer of the stomach can be found, every physician should remember that at the present time the only known cure for the disease is early radical surgical removal. He should make an effort to establish the diagnosis promptly. The surgeon should do his part by preparing his patients carefully for operation, and by carrying out a complete and careful surgical excision in accordance with the principles used in the treatment of cancer in other locations, and with a clear knowledge of the anatomical features which are involved.

M. M. ZINNINGER.

MEMOIRS

GEORGE CRILE

1864–1943

ONE of the most remarkable careers in the history of American surgery came to a close in the death of Dr. George Crile at the Cleveland Clinic Hospital on January 7, 1943. The fatal illness was due to subacute bacterial endocarditis and Streptococcus faecalis septicemia.

Dr. Crile was born in Chili, Ohio, November 11, 1864, the son of Michael and Martha Deeds Crile. He graduated from Ohio Northern University and from Wooster Medical School, now Western Reserve University, in 1887. During the next two years he studied in Vienna, Paris, and London, and upon his return became lecturer and demonstrator in histology and subsequently professor of principles and practice of surgery at Wooster University. He was professor of surgery at Western Reserve University and surgeon to the Lakeside Hospital from 1911 to 1924. In 1921, he and his associates established the Cleveland Clinic and, in 1924, completed the Cleveland Clinic Hospital.

Dr. Crile's life was one of amazing energy, which he maintained up to the time of his final illness. It was not surprising that a man of such personality, of such initiative, driving power, and independence of thought should have become known throughout the entire surgical world. His capacity for making friends, his infectious enthusiasm, his optimism, and his unfailing courtesy to his assistants and his staff made visitors to his clinic as welcome as he himself was wherever he traveled. His diversity of interests and accomplishments provides unlimited material for a biographical sketch, but it is only possible to refer briefly to those activities which will be accepted as representing at least some of his noteworthy achievements.

As a surgeon, Dr. Crile's reputation was based on unusual professional attainments and personal attributes. He was a master craftsman and exponent of the art of surgery. It was this superlative technical skill and all that it implied which led to his investigations as to the causes of surgical shock and the means of its prevention. The theory and practice of anoci-association were the result. Surgeons accepted this in principle but they were also aware that the primary factor in reducing surgical trauma to a minimum was the consummate skill with which he carried out every operation. In this one respect alone, Dr. Crile contributed immeasurably to the advancement of surgery in this country, as did the late Lord Moynihan in the same way in Great Britain.

Conspicuous in Dr. Crile's achievements in surgery was his pioneer work in the surgery of the endocrine system, particularly in the surgical treatment of diseases of the thyroid and parathyroid glands. In this field, his experience was enormous. His inquiring mind found ample scope in the physiology of the endocrine system and his efforts to connect disorders of this system with other diseases and to attempt to control them by surgical procedures have been one of the most stimulating chapters in medicine. It was this curious desire to explore the unknown together with his great surgical skill which made Dr. Crile such a unique figure in the surgical profession.

The writings of Dr. Crile are an accurate measure of his range of activities and interests. His early papers were concerned chiefly with results of his surgical experience and, as were other clinical surgeons of his day, he was constantly searching for safer techniques. The operative procedures which he developed and the clarity with which he described them had much to do with the development of surgery during his lifetime. The more important contributions were his method of direct blood transfusion, the technique of thyroidectomy, laryngectomy, the removal of esophageal diverticulum, biliary operations, and the operative procedures on the gastrointestinal tract. As the sequence of his publications is followed, one will find evidence of the theory that the human organism is an electrochemical mechanism and his studies of the interrelation of the thyroid gland, the suprarenal glands, and nervous system from both a clinical and experimental standpoint became the basis for an approach to the problems of hyperthyroidism, peptic ulcer, and essential hypertension. With all this activity in research, he continued to contribute authoritatively the results of his vast experience in surgery of the thyroid gland, in the surgical management of cancer in various situations, and in diseases of the gall bladder. Throughout all his writings, one will find a constant effort to reduce mortality and morbidity of operations, and it was in the application of these principles that he contributed so greatly to his own fame and to the prestige of American surgery.

The development, in 1921, of the Cleveland Clinic and Foundation is a story of a group of men who throughout all their professional lives had been associated in medical practice and thus developed a rapidly growing nucleus of organization. These men were the late Dr. F. E. Bunts, Dr. Crile, and Dr. William E. Lower, all of whom had been engaged in teaching in the medical school in Wooster University and in Western Reserve University and who had been colleagues in the organization of the Base Hospital of Lakeside Hospital which was attached to the American Expeditionary Force in the first World War. When this unit returned to the United States in 1919, the Cleveland Clinic was organized and has provided such splendid facilities for sound clinical practice, research, and education of graduate students as to bring world reknown to Dr. Crile and his associates.

No greater evidence can be found of Dr. Crile's amazing vitality than his ability, with all the responsibility of organizing the Clinic and Foundation, to give his time and interest to so many professional societies and associations. He was particularly active in the American Surgical Association of which he was president in 1923, in the Southern Surgical Association and in the Association for the Study of Goiter. He was a member of the editorial board of SURGERY, GYNECOLOGY AND OBSTETRICS, from 1920 to 1942, and also held similar offices in other scientific journals.

Dr. Crile was one of twelve men, who in 1912 formed a committee for the organization of the American College of Surgeons. He became a member and eventually chairman of the first Board of Regents, a position he held until his resignation in October, 1939, when he passed on the chairmanship to Dr. Irvin Abell. Dr. Crile was president of the College in 1916–17 and upon his resignation as a regent in 1941, he was appointed to the Advisory Council. At the death of Dr. Franklin Martin, who had been Director General of the College until 1935, Dr. Crile gave liberally of his time and support to the work of the College, particularly in respect to such activities as hospital standardization, clinical research, and publications. He saw, as did others, that there was needed in this country a society of surgeons more inclusive than those societies of limited membership, and that such an association could do much to give more skilled surgical care to the American people. The approach to this was sound as it was based on according fellowship in the College to those surgeons who, eight years or more after graduation from medical school, had demonstrated to their colleagues and to the State Committees of the College that they were competent surgeons. The purposes and ideals of the College in which Dr. Crile so sincerely believed were well expressed by Dr. Crile himself in the Annual Oration on Surgery at the San Francisco Clinical Congress in 1935:

"It should be borne in mind that we are building not in the interest of the profession but primarily in the interest of the people at large. The automobile, the airplane, and other methods of transportation, the machinery of civilized man, is so distributed on the farms and ranches, in the mines, on the highways, on railways and in the air, that everybody is on the front line so that in the case of an accident, a disease, or a surgical operation, it is as necessary to have a good surgeon in the most remote place as it is to have one in San Francisco, Los Angeles, Boston, New York, or Philadelphia. Therefore, our task is to see to it that there are good surgeons all over Canada and the United States; and wherever there is a human being who requires the service of a surgeon, we must have a good surgeon and a good hospital."

An example of Dr. Crile's broad experience in surgical organizations is the fact that he was a charter member in the Society of Clinical Surgery which was organized in 1903 and the first meeting was held in Baltimore. The meetings also included visits to clinics in Great Britain and the continent. At the last Cleveland meeting in 1936, the members will, I am sure, never forget the drama of seeing Dr. Crile, at the age of seventy-two years, perform celiac ganglionectomy for hypertensive disease.

Dr. Crile was an important factor in making the Interstate Postgraduate Association of North America the outstanding course of postgraduate instruction in the world. This association has set such a splendid example of what can be accomplished that several similar organizations have been formed. Dr. Crile's part in the development of the Interstate Postgraduate Association was recognized by the presentation of a medal at special ceremonies in 1937.

Dr. Crile's war record is as conspicuous as any of his varied activities. He served during the Spanish-American war as a Brigade-Surgeon in the Porto Rican Campaign. He was one of the first group of physicians appointed to the Medical Reserve Corps and served as special professor at the Army Medical School, Washington, D. C., during 1913–14. During the first World War, Dr. Crile in his civilian capacity, served as surgical director of the American Ambulance Hospital (The Lakeside Unit) in France and returned to the United States to become director in charge of the staff of Base Hospital No. 4, which was organized under the auspices of the Lakeside Hospital. This was the first unit of the United States Army to reach Europe, and it remained with the British Expeditionary Forces in France during its entire overseas existence and operated as No. 9 General Hospital. When this unit was demobilized in 1919, Major Crile was assigned as senior consultant in surgical research and as clinical director. At the close of the World War, he was appointed Colonel in the Medical Reserve Corps and was also cited for distinguished service by the British government in a dispatch from Field Marshal Sir Douglas Haig. He was appointed Brigadier General in the Medical Reserve Corps in 1921 and was awarded the Distinguished Service Medal and in awarding this medal, the Commanding General said of Dr. Crile: "By his skill, researches and discoveries, he saved the lives of many of our wounded soldiers. His tireless efforts to devise new methods of treatment to prevent infection and surgical shock revolutionized Army surgery and met with the greatest success." In the present war, Dr. Crile was made honorary consultant to the Medical Department of the United States Navy.

Dr. Crile's pre-eminence in the surgical world is evidenced by the honorary degrees, citations and awards he received from the highest educational institutions. As he advanced in years Dr. Crile began to devote more of his time to recreation and travel, and even in these later activities his interest in scientific medicine and research continued. It was during these travels that Dr. Crile collected great numbers of sea and land animals from all parts of the world and observed the differences in power and personality of these animals in relation to the comparative sizes of the brain, thyroid gland, suprarenal glands, and sympathetic nervous system. In 1935, he donated to the American College of Surgeons an extensive exhibit of many of his specimens which duplicated one in Cleveland. In the winter of 1923–24, he organized and conducted an ornithological expedition to the tip of southern Florida and in 1935, with Mrs. Crile, he made a trip

to Africa to make a study of wild life. The fascinating story of this trip is told in a book written by Mrs. Crile, entitled *Skyways to a Jungle Laboratory: an African Adventure.*

The passing of Dr. Crile will be mourned by his colleagues, his associates, and his assistants, and the surgical profession of the world will pay tribute to the influence of a superb surgeon, a great organizer, an indefatigable and original worker and a buoyant and stimulating personality.

DONALD C. BALFOUR

CRILE, GEORGE

Born in Chili, Ohio, November 11, 1864; son of Michael and Margaret (Dietz) Crile
Died, Cleveland, January 7, 1943
Married Grace McBride of Cleveland, February 7, 1900
Children: Margaret (Mrs. Hiram Garretson), Elisabeth (Mrs. J. A. Crisler, Jr.), George, Jr., Robert
Ohio Northern University, A.B., 1884; A.M., 1888
Wooster University (Western Reserve University), M.D., 1887; A.M., 1894; LL.D., 1916
Postgraduate study in Vienna, 1893; London, 1895; Paris, 1897
Honorary degrees: Hiram College, Ph.D., 1901; University of Dublin, M.Ch., 1925; University of Glasgow, LL.D., 1928; University of Guatemala, Doctor *honoris causa*, 1939
Lecturer and Demonstrator of Histology, 1889, 1890; Professor of Physiology, 1890–1893; Professor Principles and Practice of Surgery, 1893–1900, Wooster University
Professor of Clinical Surgery, 1900–1911; Professor of Surgery, 1911–1924; Emeritus Professor of Surgery, 1924–1943, Western Reserve University
Visiting Surgeon, Lakeside Hospital, 1911–1924
Founder and director, Cleveland Clinic Foundation, 1921–1943
Surgeon, Cleveland Clinic Hospital, 1924–1943
Member of Editorial Board, SURGERY, GYNECOLOGY AND OBSTETRICS, 1920–1942; member Board of Directors, Surgical Publishing Company of Chicago, 1935–1942
Brigade Surgeon of Volunteers, Major, Cuba and Puerto Rico campaign, 1898; Major Med. O.R.C. and director, U.S.A. Base Hospital No. 4, Lakeside Unit (B.E.F., No. 9) in France, May, 1917—May, 1918; Senior Consultant in Surgical Research, May, 1918—January 1919; Lieutenant Colonel, M.C. June, 1918; Colonel, November 1918; Brigadier General, Med. O.R.C., 1921
Awarded Distinguished Service Medal (U.S.) 1919; honorary member Military Division 3d class, Companion of Bath (British), 1919; Chevalier Legion of Honor (French), 1922. Alvarenga prize, College of Physicians, Philadelphia, 1901; Cartwright prize, Columbia University, 1897 and 1903; Senn prize, American Medical Association, 1898; American medal for service to humanity, 1914; National Institute Social Sciences medal, 1917; Trimble lecture medal, 1921; 3d Laureate of Lannelongue Foundation medal, Société Internationale de Chirurgie de Paris, 1925; Cleveland medal for public service, 1931.
Memberships in medical and other organizations. American Association Anatomists; American Association for the Advancement of Science; American Surgical Association —president, 1923; American College of Surgeons—president, 1916, member organizing committee, Regent, Chairman Board of Regents, member Advisory Council Board of Regents, 1941–1943, and member of Cancer Committee, Committee on Hall of Art and Science, Committee on Inter-American Relations, Medical Motion

Pictures, Co-operating Committee with American College of Physicians; American Medical Association; American Physiological Society: American Association of Obstetricians, Gynecologists and Abdominal Surgeons; Southern Surgical Association; Southern Medical Association; American Philosophical Society; Association American Pathologists and Bacteriologists; Society of Clinical Surgery; Society of Experimental Biology and Medicine; National Institute of Social Sciences; National Research Council; Association for the Study of Internal Secretions; American Heart Association; American Medical Editors' Association; Ohio State Medical Association; Cleveland Academy of Medicine; Cleveland Medical Library Association; American Association for the Study of Goiter; American Board of Surgery, Founders Group; Interstate Postgraduate Medical Association of North America; Union Club of Cleveland; and of various American and European societies.

Books. Surgical Shock, 1897; Surgery of the Respiratory System, 1899; Certain Problems Relating to Surgical Operations, 1901; On the Blood Pressure in Surgery, 1903; Hemorrhage and Transfusion, 1909; Anemia and Resuscitation, 1914; Anoci-Association (with Lower), 1914; 2d. ed. title, Surgical Shock and the Shockless Operation through Anoci-Association, 1920; Origin and Nature of the Emotions, 1915; A Mechanistic View of War and Peace, 1915; Man, An Adaptive Mechanism, 1916; The Kinetic Drive, 1916; The Fallacy of the German State Philosophy, 1918; A Physical Interpretation of Shock Exhaustion and Restoration, 1921; The Thyroid Gland (with others), 1922; Notes on Military Surgery, 1924; A Bipolar Theory of Living Processes, 1925; Problems in Surgery, 1928; Diagnosis and Treatment of Diseases of the Thyroid Gland (with others), 1932; Diseases Peculiar to Civilized Man, 1934; The Phenomena of Life, 1936; The Surgical Treatment of Hypertension, 1938.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

A SUMMARY is presented in *Nutrition and Chemical Growth in Childhood*[1] by Icie G. Macy, Ph.D., of the research work in biochemistry of childhood carried out by the Children's Fund of Michigan under the directorship of the author. Volume I, *Evaluation*, is a book of 381 pages. Volume II, *Interpretation*, has not yet been published.

The present volume is very well arranged giving many of the laboratory results of the author's experiments. It is profusely illustrated. The last third of the book is taken up almost exclusively with laboratory methods and the treatment of scientific data. The book is not in any sense a summary of the world's literature on the subject, being, rather, a conscientious report of the author's experiments. It can, therefore, be recommended as a source book of information on the extensive studies made by the Children's Fund of Michigan. For those interested in laboratory methods and research on this subject it provides excellent material. The second volume, not yet published, in which Dr. Macy will discuss the interpretation of her findings should be of wider interest to the general reader.

C. ANDERSON ALDRICH.

A TREATISE on the art of looking at the surgical patient with a seeing eye is presented in *Demonstrations of Physical Signs in Clinical Surgery*[2] by Hamilton Bailey. Many signs of disease and methods of examination overlooked by the inexperienced or careless surgeon are illustrated by pertinent text and excellent illustrations, both of which reflect a sound knowledge of the underlying pathological condition and the relative importance of physical diagnostic methods.

Mr. Bailey's book is a worthy successor to De Quervain's *Surgical Diagnosis*, which for many years was a classic in this field.

While strictly speaking there is no bibliography given, a very attractive feature consists in referring in footnotes to the names of medical men whose names are associated with clinical signs, complexes, or methods of examination, often giving their birth dates, places of residence, and positions which they held.

Particularly valuable chapters are devoted to the diagnosis and pictorial characteristics of various lesions of the neck, salivary glands, and thyroid. The chapter on lesions of the male genitalia reflects particular interest and skill on the part of the author in this particular field.

The whole book is excellently edited and printed and is pleasant to read.

The author holds most properly that the use and appraisal of physical methods of examination coupled with the detection of visual signs of disease should precede special laboratory methods or surgical exploration in diagnosis. He has successfully selected, described, and depicted these methods and signs which with intelligent use add the Sherlock Holmes touch to surgical diagnosis. VERNON DAVID.

TO cover the broad field of infections, injuries, fractures, repair of nerves and tendons, congenital deformities, tumors and "diseases" of the hand in a single volume is an ambitious task, and Cutler has accomplished it very well in his *The Hand; Its Disabilities and Diseases*.[3]

The section on specific and chronic infections of the hand (Chapter III) is particularly well done and well illustrated. The chapter on burns is disappointing in that it does not omit the many "half hearted" methods of treatment and bring out in clear cut fashion the importance of securing a clean granulating surface at the earliest possible moment and covering areas of whole thickness loss with grafts of intermediate thickness.

The section on incised and lacerated wounds is well done. One would wish more emphasis had been laid on the importance of a bloodless field and of incisions which avoid cutting across flexion creases. (The same comment might be made concerning the discussion of the care of infections.)

Chapters on fractures, dislocations, repair and reconstruction and tumors are well written and well illustrated. All in all the author has drawn on his own extensive experience and on that of others to produce a very readable and a helpful contribution to the subject of hand surgery. SUMNER L. KOCH.

[1] NUTRITION AND CHEMICAL GROWTH IN CHILDHOOD. VOLUME I—EVALUATION. By Icie G. Macy, Ph.D., with a foreword by Hugo A. Freund, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1942.

[2] DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY. By Hamilton Bailey, F.R.C.S. (Eng.). 8th rev. ed. Baltimore: Williams & Wilkins Co., 1942.

[3] THE HAND; ITS DISABILITIES AND DISEASES. By Condict W. Cutler, Jr., M.D., F.A.C.S. Philadelphia and London: W.B. Saunders Co., 1942.